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INTERPRETATION OF THE ELECTROMYOGRAM

D. DENNY-BROWN, M.D.
BOSTON

IN RENEWING electromyographic investigations of human muscles after an interval, I find that considerable differences of opinion have accumulated in regard to the interpretation of several electromyographic changes encountered in neurologic disorders. Since electromyography is in common use in some clinics and can provide useful diagnostic information, it may be of general interest to discuss critically some of the fundamental principles involved in the method.

Early work on the action potentials of muscle has been reviewed by others,[1] and Pennybacker and I[2] previously discussed at length the relation of action potentials of single muscle fibers to those series of much larger rhythmic variations which are associated with the natural discharge of a single motor nerve cell. Physiologically, the "motor unit" is defined as a motor cell, its axon process and the group of muscle fibers which this one cell innervates. The rhythmic pattern of electrical changes (action potentials) in the discharge of single motor units in the earliest phase of a voluntary contraction of human muscle can be recorded with ease by a variety of methods, even with skin electrodes and an ink-writing electroencephalographic machine. A fundamental question is the extent to which a rhythmic series of identical fluctuations in potential can safely be interpreted as the discharge of

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From the Neurological Unit, Boston City Hospital; the Department of Neurology, Harvard Medical School, and the National Hospital for Nervous Diseases, Queen Square, London, England.

1. (*a*) Adrian, E. D.: Interpretation of the Electromyogram, Lancet **1**:1230-1233; **1**:1281-1286, 1925. (*b*) Wachholder, K.: Willkürliche Haltung und Bewegung, Ergebn. d. Physiol. **26**:568-775, 1928. (*c*) Smith, O. C.: Action Potentials from Single Motor Units in Voluntary Contraction, Am. J. Physiol. **108**:629-638, 1934. (*d*) Lindsley, D. B.: Electromyographic Studies of Neuromuscular Disorders, Arch. Neurol. & Psychiat. **36**:128-157 (July) 1936. (*e*) Hoefer, P. F. A., and Putman, T. J.: Action Potentials of Muscles in Normal Subjects, ibid. **42**:201-218 (Aug.) 1939. (*f*) Weddell, G.; Feinstein, B., and Pattle, R. E.: The Electrical Activity of Voluntary Muscle in Man Under Normal and Pathological Conditions, Brain **67**:178-257, 1944. (*g*) Cobb, S.: Review of Neuropsychiatry for 1945, Arch. Int. Med. **77**:576-591 (May) 1946.

2. Denny-Brown, D., and Pennybacker, J.: Fibrillation and Fasciculation in Voluntary Muscle, Brain **61**:311-334, 1938.

a single unit in more powerful contractions or in pathologic states. It is essential to determine to what extent the abnormal behavior of electrical rhythms can be related to abnormality of the motor cell itself and what changes can be correlated with alterations in the synapse or in supranuclear structures. In clinical use, electromyography lacks the facility for control experiments such as the experimental physiologist can readily devise by such procedures as decerebration, section of nerve roots or isolation of muscles by nerve section. As the following discussion will reveal, too little is known of the normal behavior of muscles and of the process called "willed movement" to permit the deductions that some investigators have claimed on the basis of differences seen in the electromyogram in disease.

METHODS

It is not proposed to discuss here the electrical problems of the amplifiers used. Various physiologists have published electrical circuit diagrams. Nor is it necessary to describe the numerous varieties and arrangements of electrodes which I have been using. For some purposes, surface electrodes of the type used in electroencephalography have been adequate to give a general total electromyographic picture of a region or to record the effects of nerve stimulation in a whole muscle group, such as those of the hypothenar eminence. Such electrodes avoid the mechanical changes which the presence of a needle in muscle provokes and which may be prominent in conditions of increased muscular irritability, such as myotonia. For the study of single units or a small group of units, a concentric needle electrode of the type originally used by Adrian and Bronk [3] was employed. It is instructive to use loose insulated wire as core lead, the wire protruding through a hypodermic or larger needle, which forms the indifferent lead. The extent of the sampled field can then be varied by altering the degree of protrusion of the core. The use of "bakelite" or similar enamel or plastic allows independent sterilization of the core wire. It will be found, however, that single units can more readily be isolated when the core wire does not protrude from the needle, but presents its bared surface only at the lumen. The records presented in this paper were obtained with such an arrangement, silk-covered copper wire coated with hardened bakelite [2] varnish being used. My colleagues and I now use a needle with fixed core, similar to that described by Pritchard,[4] Smith,[1c] Lindsley [5] and others, and find that very fine silver wire (45 standard wire gage) gives less polarization and injury current.

The low frequency response of standard ink-writer recorders renders difficult the differentiation of similar motor units in a mixed pattern, for the finer differences in wave shape are slurred. The very rapid, small waves of fibrillation can be recorded with such an instrument but bear a close resemblance to artefact at the high amplification required to record them. For more accurate work galvanometers

3. Adrian, E. D., and Bronk, D. W.: The Discharge of Impulses in Motor Nerve Fibres: II. The Frequency of Discharge in Reflex and Voluntary Contractions, J. Physiol. **67**:119-151, 1929.

4. Pritchard, E. A. B.: Electromyographic Studies of Voluntary Movements in Paralysis Agitans, Brain **52**:510-529, 1929; The Electromyogram of Voluntary Movements in Man, ibid. **53**:344-375, 1930.

5. Lindsley, D. B.: Electrical Activity of Human Motor Units During Voluntary Contraction, J. Physiol. **114**:90-99, 1935.

recording by reflected light on moving film or bromide paper are necessary. In the present study, based on records made in the National Hospital, London, from 1935 to 1939, Matthews galvanometers were used. Other investigators have used the Duddell galvanometer [1d] or have photographed the image of a cathode ray oscillograph.[1f] A moving bromide paper strip or film record has the advantages of allowing prolonged records and the addition of a tracing of the mechanical contraction. For the latter, I have used reflected beams of light from the membrane of a manometer which was actuated by air under pressure connected by rubber pressure tubing to a balloon. The balloon was embedded in a sponge for recording grasp or applied to the belly of the muscle and covered with a small box, which was, in turn, held to the skin by adhesive tape.[2]

Electromyography shares with electroencephalography the difficulty in prediction of the type and shape of electrical change recorded from any point in a semifluid, three dimensional medium when electrical changes of known shape are introduced into another part of the medium. The difficulty is the greater because, though much is known of the electrical change accompanying excitation when nerve or muscle is surrounded by a nonconductor, the short circuiting provided by contiguous active or inactive muscle elements and connective tissue is problematic. Those who employed early methods of recording muscle potentials from the exposed muscle of animal preparations by two pins inserted directly into the muscle belly with direct leads to a string galvanometer [6] will be familiar with the effective short circuiting provided by the superficial connective tissue. This tissue, or perimysium, then had to be cleared carefully before any recognizable record could be obtained. With electronic amplification this difficulty is overcome, but an enormous connective tissue shunt clearly must be incorporated in the field from which the voltmetric record is derived. The small change in voltage which the electrocardiogram undergoes at various distances from the immediate proximity of the heart indicates that this must be so. The importance of this appears in the consideration of spread of certain effects, particularly in atrophic, fibrotic muscle. Such spread of effect allows the recording of isolated motor units from surface skin electrodes, but it also means that electrical recordings from different muscles, such as concurrent activity in antagonists, must be scrutinized with great care before the amount of electrical independence can be determined. Careful visual observation of the muscles concerned is a necessary control.

It has been the experience of all investigators in this field that a prominent single active motor unit can be found isolated in inactive muscle with a needle electrode, and Weddell and associates [1f] hold that such a unit could be localized to within 10 mm. by advancing or withdrawing a coaxial needle. The beveled tip gave some directional indication, so that rotation of the needle varied the amplitude from maximum to zero. Such observations undoubtedly indicate that, in some circumstances, unit discharge can be strictly localized in its transverse diameter. The experiments of Adrian [7] on the tenuissimus muscle of the cat showed not only that the action potential spreads lengthwise along the muscle fiber but that the overlapping of fibers of the same unit will give a polyphasic action current. The electrical unit, therefore, must have a length of 2 to 10 cm. or more. Experience

6. (*a*) Forbes, A., and Barbeau, A.: The Question of Localizing Action Currents in Muscle by Needle Electrodes, Am. J. Physiol. **80**:705-715, 1927. (*b*) Denny-Brown, D.: On the Nature of Postural Reflexes, Proc. Roy. Soc., London, s.B **104**:252-301, 1928.

7. Adrian, E. D.: The Spread of Activity in the Tenuissimus Muscle of the Cat and in Other Complex Muscles, J. Physiol. **60**:301-315, 1925.

with the decerebrated animal when the recording muscles can be dissected and explored at will, however, has convinced me that if a muscle is the seat of an intense discharge its electrical activity can be recorded with ease from totally inactive or denervated muscles 10, or even 15, cm. away. This is also clear in the ease with which action potentials in the eye and facial muscles can be recorded from different parts of the head in man during electroenphalographic records. The spread of the electrical field is purely relative and, apart from the size of the electrode and the sensitivity of amplification, is greatly influenced by the size of the motor unit and its relation to connective tissues. The only direct control of the size of the motor unit is measurement of the mechanical contraction it produces.

OBSERVATIONS

Size of the Human Motor Unit.—In an earlier paper,[2] various types of twitching of muscles observed in clinical neurology were analyzed electromyographically, and a distinction was made between "true fibrillation," or the very small flickerings of muscle totally paralyzed by nerve section, and the twitching of bundles of muscle fibers for which the name "fasciculation" was proposed.

True fibrillation is generally visible to the eye only in very superficial muscles, such as those of the tongue, and is accompanied with an asynchronous series of very rapid and uniformly small action potentials. Reasons were advanced for these potentials, which occur in single muscle fibers, where they repeat rhythmically after the eighth to twelfth day of degeneration. Similar small potentials can be recorded in the conditions of changed muscular irritability, such as that due to mechanical irritation of a myotonic muscle or the drying of an exposed surface of normal or excised muscle. The electromyography of fibrillation has been developed as a valuable aid in the diagnosis of peripheral nerve lesions, both in cases in which true muscular atrophy is in doubt and in the recognition of the earliest regeneration by disappearance of the fibrillation.[1f] The differential diagnosis of laryngeal paralysis and cricoarytenoid arthritis by means of electromyography [1f] is a remarkable feat. Electromyography is of value in the recognition of block of nerve conduction due to an ischemic lesion, such as occurs in mild types of facial palsy or in some types of damage to the brachial plexus by dislocation of the shoulder or by pressure between the clavicle and the first rib as a result of prolonged malposition, by tourniquet paralysis and by simple pressure palsy. Here, motor block may be absolute, and yet fibrillation may not occur.[8] The situation, one finds, is seldom clearcut, and more aid is to be expected from a general estimation of the amount of fibrillation present from the second week onward, in relation to the deficit in motor power, than from flat differentiation into fibrillating and nonfibrillating paralysis.

8. Denny-Brown, D., and Brenner, C.: Paralysis of Nerve Induced by Direct Pressure and by Tourniquet, Arch. Neurol. & Psychiat. **51**:1-26 (Jan.) 1944.

Fasciculation is a more complex subject. In an earlier study,[2] the characteristics of several types were defined, from the localized repetitive discharges of altered metabolic states to the commonly observed flickering of the muscles (previously known as "fibrillation") associated with progressive muscular atrophy and amyotrophic lateral sclerosis (motor neuron disease). Analysis of the phenomenon in these diseases indicated that the twitching then resulted from abnormal nerve impulses in motor units and that such units discharged spontaneously and rhythmically at intervals of two to ten seconds. Each abnormal discharge resulted in a twitch of all the muscle fibers of the unit, and the resulting electrical and mechanical disturbance was characteristic for that unit. Such units were still able to be activated by voluntary contraction, and the spontaneous discharge was not affected by inhibitory processes. With each advance of the disease such fasciculation becomes more intense, but as neuronal degeneration occurs the muscle fibers atrophy and an increasing proportion of "true fibrillation" is present.

It has been shown by Swank and Price [9] and others that procaine block did not prevent the coarse fascicular twitches. Forster, Borkowski and Alpers [10] recently reported that section of the motor nerve in cases of advanced amyotrophic lateral sclerosis is followed by a similar frequency of fasciculation in the muscle concerned for the few days before the ensuing wallerian degeneration and true fibrillation become general. These experiments indicate that the abnormal impulses can take origin in the peripheral portion of the motor nerve. Yet the usual site of origin of these abnormal discharges is still in doubt. The nerve cell certainly undergoes a primary histologic change, and I prefer to regard this disease as the outcome of disorder of the whole excitable cell membrane rather than to postulate separate peripheral and central factors in its mechanism. The physiologist finds no essential qualitative difference between the excitability of the synapse and that of the axonal membrane. The neuropathologist, likewise, may find that the true explanation of progressive muscular atrophy rests in a disorder of enzyme activity underlying the excitability of the motor neuron as a whole. The fasciculation produced by neostigmine is especially significant in this connection, for the abnormal excitation is known to have a peripheral origin, spreading centripetally through the ramifications of the motor nerve cell. In human muscle, fasciculation due to neostigmine is of smaller amplitude and more directly follows use of the muscle than does that of motor neuron disease.

9. Swank, R. L., and Price, J. C.: Fascicular Muscle Twitchings in Amyotrophic Lateral Sclerosis: Their Origin, Arch. Neurol. & Psychiat. **49**:22-26 (Jan.) 1943.

10. Forster, F. M.; Borkowski, W. J., and Alpers, B. J.: Effects of Denervation of Fasciculations in Human Muscle: Relation of Fibrillations to Fasciculations, Arch. Neurol. & Psychiat. **56**:276-283 (Sept.) 1946.

Further, it tends toward repetitive volleys. These features also characterize the fasciculation which follows ischemia produced by tourniquet. The similar slowness of each undulation of myokymia is appreciable to the eye, owing to similar repetitive discharges, as I have pointed out elsewhere.[2] These features still serve as an aid in the differentiation of these other types of fasciculation from that of motor neuron disease.

It appears now to be generally accepted that the fasciculation of amyotrophic lateral sclerosis and progressive muscular atrophy is the result of spontaneous single excitatory impulses in abnormal motor units. If such fasciculations are studied closely, they afford considerable information as to the size and distribution of such units in man, as well as give valuable control of the electromyographic method. In cases of progressive muscular atrophy it is apparent to the unaided eye that the individual twitches of different units vary greatly in size but little in duration. These differences may be recorded by sensitive technics.[2] In figures 1 *A* and *C* and 2 *A* and *D*, it is seen that the units of the twitch of human muscle follow much the same course as that in the gastrocnemius muscle of the cat, reaching half-relaxation in approximately $\frac{1}{10}$ second. In some muscles twitches with a duration as short as 70 milliseconds have been recorded (fig. 2 *A*). It can be observed by inspection in the clinic that twitchings of both large and small units are present in all muscles, but that even the smallest of the twitchings of the shoulder and pelvic girdle all appear to be relatively coarse. Even the intrinsic muscles of the hand present twitches from some very large units, capable alone of evoking movement of the thumb or finger. The units in the biceps brachii and pectoralis muscles, in particular, are very long, extending to 10 cm., and in most muscles to 5 cm. The electrical disturbance of large units can be also very large, with readings up to 1 or 2 millivolts, and are often polyphasic in shape. The action potential at first decreases rapidly in size and lengthens in duration as the needle is withdrawn from the immediate neighborhood of the observed recurrent twitch, but the electrical variation can be recorded from distant parts of the muscle, often from unrelated and quiescent muscle 10 cm. or more away. This transmissibility appears to be related to the size of the disturbance, for it does not occur with the smaller units. The spike potential is slower in all phases as the distance from its source of origin increases.

The concurrent recording of the mechanical and electrical phenomena of contraction in human muscle also reveals that there is no difference between the spontaneous twitches of fasciculation and minimal tendon jerks (fig. 2 *A*). Both can be accepted as evidence that the twitch, or minimal contraction process, in human muscle follows the same form and time reactions as that in the slower muscles of the cat and monkey. It is further seen that the fusion of twitching into a fairly smooth

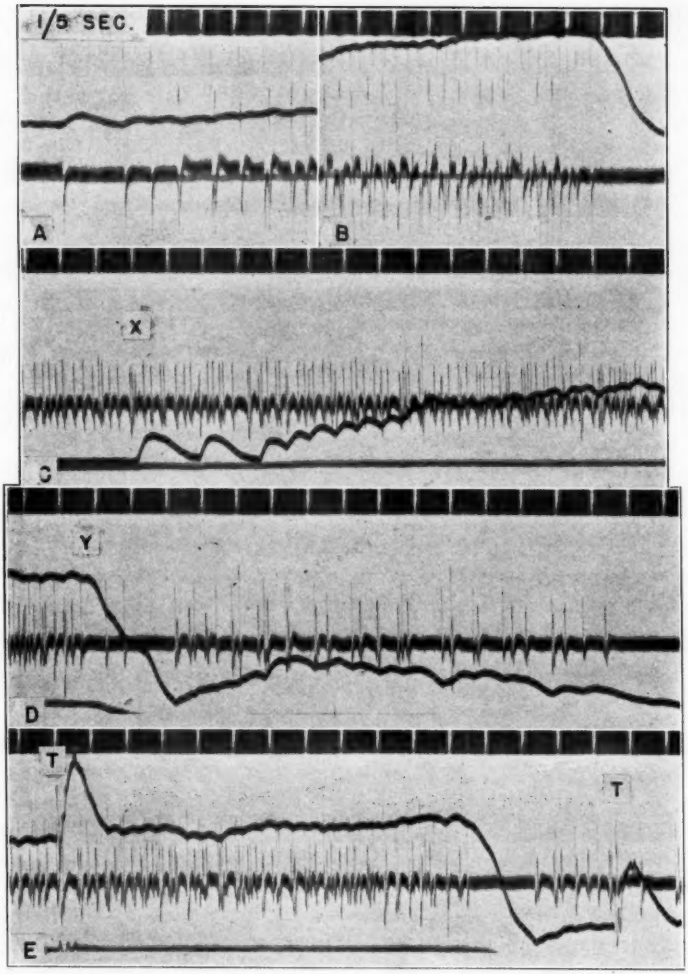

Fig. 1.—*A*, tracings from the biceps brachii muscle in a patient with progressive muscular atrophy during voluntary flexion of the elbow. The mechanical record traces swelling of the muscle belly, recorded by a balloon attached over it. The electromyogram shows two motor units, one giving three action currents before the other begins to discharge. Time intervals of 1/5 (0.2) second are shown by vertical white lines at the top of the figure.

B, continuation of the discharge commencing in *A*, after an interval of 1.5 second, showing the contraction reaching a plateu and its abrupt cessation when the patient was told to relax.

C, tracing from another part of the biceps in the same patient. One unit is already discharging, when, in response to voluntary effort, an additional unit begins discharge at *X*, and the result of increase of frequency in its discharge is recorded.

D, continuation of the discharge shown in *C* after the lapse of 2.0 seconds. The patient relaxes at *Y*, but discharge in the three units shown in *C* is renewed. The tracing illustrates the extent to which the mechanical twitching of large units is damped by that of small units.

E, tracing from the same muscle of the same patient, showing the effect of superimposed tendon jerks at *T* and *T*.

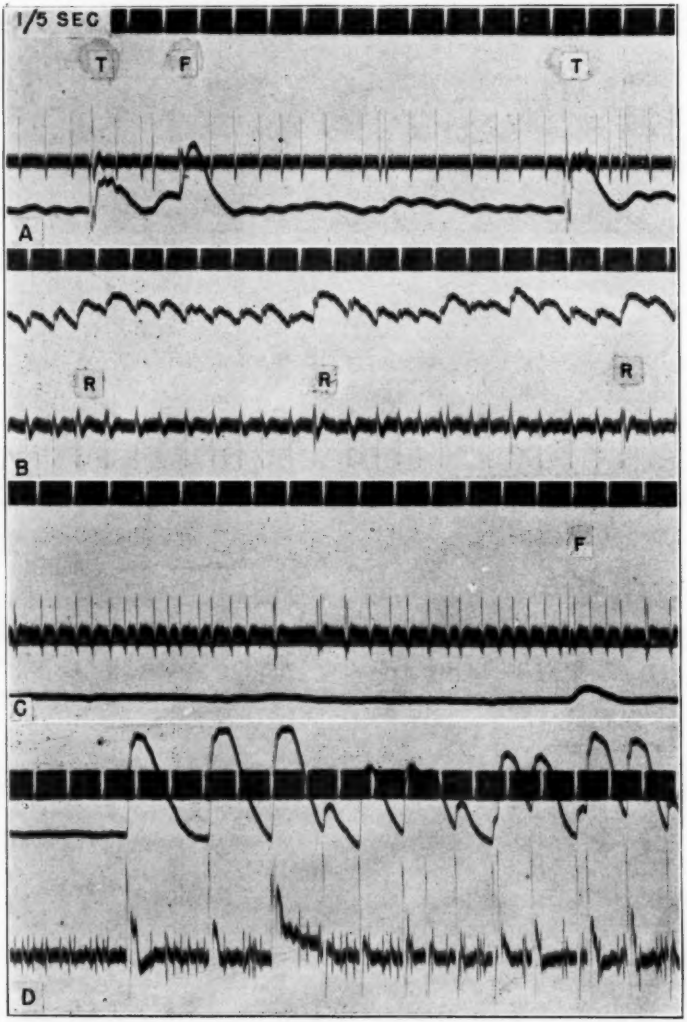

Fig. 2.—*A*, mechanical record and electrical action currents of one small motor unit of the biceps brachii muscle of a patient with progressive muscular atrophy during incompletely relaxed posture, with two tendon jerks (*T*, *T*) and one spontaneous twitch of fasciculation (*F*).

B, continued discharge of the extensor communis digitorum of a patient with progressive muscular atrophy during incompletely relaxed posture, showing reduplication of the action current (which is inverted), at *R*. *R*. and *R*.

C, tracings from the biceps brachii of the same patient as the one whose record appears in *A*, but another motor unit during mild voluntary effort, showing frequent discharge from reduplication, as contrasted with a spontaneous fascicular twitch at *F*.

D, tracings from the same muscle as that discharging in *B*, showing onset of discharge of a large unit in contraction fasciculation during voluntary dorsiflexion of the wrist.

tetanic contraction occurs at a rate of discharge of about 25 a second (fig. 1 *B, C* and *D*). In figure 1 *D* it will be seen that the rhythmic discharge of one coarse unit can smooth out the otherwise prominent mechanical disturbance of another unit, though a very large twitch, such as a tendon jerk, may yet superimpose itself (fig. 1 *E*).

Absolute Synchronism in Different Units.—Recently, Buchthal and Clemmesen [11] advanced a hypothesis to explain a dominant rhythm obscured concurrently in different parts of atrophic muscles. They postulated a synchronization of rhythm of discharge in a number of different motor units on the basis of identical rhythms in three concurrent leads in the same muscle. The three amplifying and recording systems were free from mutual interaction. In a case of Charcot-Marie-Tooth peroneal atrophy the leads were more than 12.0 cm. apart and yet there was absolute synchronism. It was stated that one or another lead occasionally showed transition to independence in rhythm, but this is not illustrated. The condition was found "infrequently" in normal muscle, frequently as a result of poliomyelitis, in some cases of root compression and in 2 cases of peripheral nerve lesions. It was seen as a temporary phenomenon in spinal anesthesia.[12] It was maintained by Buchthal and Houke,[12] on the basis of their observations, that synchronization of discharge is the result of heightened permeability of contiguous motoneurons in the spinal cord and that concurrence of rhythmic discharge then takes place. It was held, therefore, that synchronism is useful in the differentiation of central and peripheral motor lesions. Indeed, Buchthal and Houcke [12] applied the criterion to prognosis and stated that in poliomyelitis "total or partial synchronization within the first 2 weeks indicates a less favorable prognosis than continuous asynchronous activity," and that "synchronization still present after the third week of the disease has a low chance of restitution."

Watkins, Brazier and Schwab [13] also noted synchronous discharges over a large extent of muscle in cases of poliomyelitis. In a later paper,[14] they mentioned its presence in cases of recovery from peripheral nerve injury and illustrated identical rhythm of discharge in tibialis and gastrocnemius muscles as evidence of "disruption of reciprocal innervation."

11. Buchthal, F., and Clemmesen, S.: On the Differentiation of Muscle Atrophy by Electromyography, Acta psychiat. et neurol. **16**:143-182, 1941; **18**:377-387, 1943.

12. Buchthal, F., and Houcke, P.: Electromyographical Examination of Patients Suffering from Poliomyelitis Followed Up to Six Months After the Acute Stage of the Disease, Acta med. Scandinav. **116**:148-164, 1944.

13. Watkins, A. L.; Brazier, M. A. B., and Schwab, R. S.: Concepts of Muscle Dysfunction in Poliomyelitis Based on Electromyographic Studies, J. A. M. A. **123**:188-192 (Sept. 25) 1943.

14. Brazier, M. A. B.; Watkins, A. L., and Schwab, R. S.: Electromyographic Studies of Muscle Dysfunction in Infectious Polyneuritis and Poliomyelitis, New England J. Med. **230**:185-189, 1944.

Hoefer and Putnam [15] also mentioned synchronization "even of smaller details of patterns," which they regarded as characteristic of spastic states. These authors proposed a theory of spread of central excitation to account for this identity of discharge and for their ability to record spike potentials from distant muscles during a tendon jerk. In all these observations, the control for the synchronous discharge in two or more leads was its absence in similar records from the normal subject.

The observations that synchronous rhythmic discharge can be recorded from larger areas in these conditions than can isolated discharges in the normal subject is not disputed. The interpretation of the phenomenon as synchronous rhythm in different motoneurons, however, is open to criticism. From the electrical aspect it is not established that the spread of effect of such normal units as initiate voluntary contraction can be assumed to hold for all units. From the purely physiologic aspect, the electrical changes should be controlled by correlation with corresponding contractile activity. Twitches or ill fused tetanic contraction should be visible, palpable and recordable whenever the theoretic spread of effect should have occurred. In the tendon jerk and in spastic clonus the muscles involved in the rhythmic twitching are readily demonstrable. In terms of muscle groups, such clonus can be seen to be strictly localized. It does not spread to opponents, to other limb segments or to the opposite limb. The crossed tendon jerk has long since been demonstrated to result from transmission of the afferent, mechanical, stretch stimulus, not the efferent volley. The "synchronization" claimed for the action current rhythm in atrophic muscle has not been demonstrated to have any corresponding visible clonus of the whole muscle, much less of its opponents.

Never in my observation has repeated absolute rhythmic synchronization of motor rhythm in different leads proved to be from two or more units by transition to independent rhythms. The nearest approach to such a phenomenon is spastic clonus, but here there is not absolute identity in successive waves. On the other hand, my colleagues and I have commonly encountered the recording of identical rhythms from different leads over wide areas in atrophic muscle even with small needle electrodes and critical, independent galvanometer systems. The condition, then, is that which I have termed "contraction fasciculation." [2] It is encountered with much greater frequency in conditions in which there have been loss of some motor neurons and partial wasting of the muscle, but it can certainly occur in peripheral nerve disease. The action current is much larger than that of the first units to enter normal willed contraction, and they can readily be picked up from a wide zone

15. Hoefer, P. F. A., and Putnam, T. J.: Action Potentials of Muscles in Spastic Conditions, Arch. Neurol. & Psychiat. **43**:1-22 (Jan.) 1940.

of the muscle, and often from neighboring inactive muscles. The accompanying twitching contraction is visible and is greater in size than that of any usually observed single unit at the beginning of a normal, voluntary movement. That the unit is a single motor cell and fiber, with its natural muscle fiber groups, is shown, however, by the consistent observation that the resultant mechanical twitching is compact and localized within the muscle belly. The resulting mechanical twitches have the same time course as those of normal units (fig. 2 *A*). If two motor cells have physical contiguity within the spinal cord so as to allow identity of discharge, it is inconceivable that their peripheral muscle units should also lie in juxtaposition. Rhythmic synchronous twitching in different parts of a muscle has not been observed.

Such large units enter and leave contraction consistently at the same stage of recruitment and have been followed for two or three hours without change. The twitching of the muscle which gives origin to their fasciculation potentials may be present for more than eight weeks without alteration. In a patient with porphyria recently under my observation, the contractions of two such units were for a time the only sign of movement in the upper limb. Their electrical activity could be picked up from almost any part of the limb segment with a coaxial electrode and ink-writing recorded. They required considerable effort on the part of the patient to innervate them. One was in the biceps brachii and one in the flexors of the fingers. As further recovery of the muscular power occurred, these tremulous units could still be seen to be present on voluntary effort, but their tremor was submerged in an earlier, smoother discharge of recovering smaller units. Yet the largest action potentials recorded from them by a coaxial lead and ink-writing system was of the order of only 300 microvolts. It is probable that the needle never made actual contact with them. Spike potentials of over 1 millivolt have been found in other cases.

The possibility that contraction fasciculation represents the result of sprouting of undamaged motor units to supply neighboring denervated muscle fibers in the early stage of the atrophic process has been considered but has been discarded, for the following reasons. First, the action potential is brief as compared with the prolonged polyphasic potential of reinnervation. Second, the tremulous mechanical twitching may be observed as early as the first week of the paralysis and thereafter does not alter for long periods.

Large units of similar size enter discharge during the phases of intense voluntary movement, though their activity is then difficult to record alone. The tremor of intense effort in fatigued muscle is certainly due to irregularity in the activity of such units. With rhythmic discharge, the resulting muscular contraction of such units begins to fuse into tetanus at the rate of about 25 impulses a second (fig. 2 *D*).

The tremulous fasciculation is therefore related to the discharge only during its low frequency of commencement. Even when the original unit continues to discharge relatively slowly, the added activity of other units smooths out the resulting mechanical contraction, as shown in figure 1 *D*. The upper limit of natural rate of rhythmic discharge which I have observed is 50 impulses a second. Higher rates are likely to occur in rebound and in other intense brief contractions, but it is then difficult to be sure that other units have not contributed. Smith,[1c] Lindsley,[1d] Seyffarth [16] Weddell and associates [1f] and others have observed rates up to a maximum of 60 impulses a second during maximum effort in partly paralyzed muscle. In voluntary contraction increase in contraction is both by increase in rate of discharge and by the participation of fresh units, as Seyffarth [16] has well shown. In spastic postural contraction, on the other hand, the rate of discharge is low, and increment is by recruitment of further units into the discharge, as in decerebrate rigidity.[6b] According to either criterion, the discharge in contraction fasciculation is natural.

In our original communication on fasciculation,[2] contraction fasciculation was defined as a variety of coarse tremulous contractions of large groups of muscle fibers arising during posture or mild effort and abolished by complete relaxation. With experience, it is possible to differentiate this condition from true spontaneous fasciculation, and from myokymia, by simple inspection of the muscles. Contraction fasciculation is clearly visible as rhythmic twitching in one part of a muscle. We have found the differentiation of considerable clinical value, for contraction fasciculation occurs in a variety of neurologic conditions in no way related to progressive muscular atrophy or amyotrophic lateral sclerosis, and yet is often confused with these diseases. It is seen in any disorder accompanied with reduction in the number of active motor units, notably, poliomyelitis, polyneuritis and injuries to nerve roots. Unfortunately, it also occurs in amyotrophic lateral sclerosis, in which I originally observed its characteristics, and is a source of confusion with true fasciculation. I prefer still to regard the phenomenon as the result of the uncovering of a normal, but very large, unit by the disappearance of many of the smaller units whose asynchronous discharge secures the natural smoothness of onset of contraction.

Reduplication of Beats and Related Phenomena.—Occasionally the rhythm of discharge is interrupted by a double wave, followed by a lengthened interval before the next wave. The "compensatory pause" resembles that of cardiac extrasystole. This phenomenon occurs at

16. Seyffarth, H.: Behavior of Motor Units in Voluntary Contraction (1940), cited by Seyffarth, H.: The Behavior of Motor Units in Healthy and Paretic Muscles in Man, Acta psychiat. et neurol. **16**:79-109 and 261-278, 1941.

times in the units of normal human subjects, and the first beat of normal unit discharge is commonly double. I observed the condition in the decerebrate animal [6b]; it was then more prominent in a deafferented muscle. In some patients with amyotrophic lateral sclerosis it has been remarkably frequent (fig. 2 *B* and *C*), but the units concerned were not fasciculating or otherwise abnormal. The additional electrical wave may occur after so brief an interval that the two waves are fused in one pattern (fig. 2 *B*). By the summation of the recorded twitch (fig. 2 *B*), and by the absence of additional mechanical activity, the mechanical record serves to indicate that the waves are in fact two beats of the same unit, and not an additional wave from another unit. An example of the effect of one impulse in an extraneous unit is shown toward the end of figure 2 *C*. A trebled response has been observed once. The pathologic significance of such a response is doubtful. I have not observed any increase in its frequency in the heightened nervous excitability of tetanus.

In some records we have observed a small, very brief spike following the primary wave at a fairly regular interval of from 10 to 15 milliseconds. This "parasite" appears and disappears as the rhythm of discharge continues (fig. 3). It is sometimes multiple, particularly after the first wave of a series, and then closely resembles "needle insertion potentials" due to mechanical muscular initiation. It is probably due to movement of the tissue against the electrode as the mechanical contraction begins, and is prominent when a disturbance of the base line gives other evidence of electrode movement, as in the second and third large responses in figure 2 *D*. The size and shape of the action current vary, of course, with the placing of the leads. In simple, single leads the unit may be formed of a chain of muscle fibers, such as Adrian [7] demonstrated in the tenuissimus muscle, with resulting complicated polyphasic wave pattern. We, therefore, do not attach any particular significance to the shape of the primary wave. In the light of these conclusions, however, the prolonged polyphasic waves commonly observed in early regeneration of motor units after nerve injury [1f] indicate a combination of diffuse innervation of muscle fibers with increased mechanical irritability.

Grouping of Discharge.—Whereas it has been concluded that the regular, exact synchronization of rhythm of discharge in two or more units does not occur, the synchronism of many different units for one beat is the basis of the single action potential of the tendon jerk.[6b] Partial synchronism or grouping is the basis of clonus and various tremors. Electromyographically, there is no difference between "true" ankle clonus (in the presence of spasticity) and "false" ankle clonus (the ankle clonus of a tense and nervous person without lesion of the central nervous system). In both types of clonus the tendon reflex is

unduly brisk, and in both there is every indication of heightened reflex activity, of which the stretch reflex is but a part. The synchronization of discharge in spastic clonus, as was shown by me [17] in cases of decerebrate rigidity, and by Lindsley [1d] in man, is not absolute, and one or another group of neurons is slightly out of step. The gaps between the beats are only relatively clear of discharge, just as the "silent period" of the tendon jerk is a relative silence. A powerful stretch reflex or other discharge can break through. The only truly synchronous stretch reflex discharge is the tendon jerk itself, when

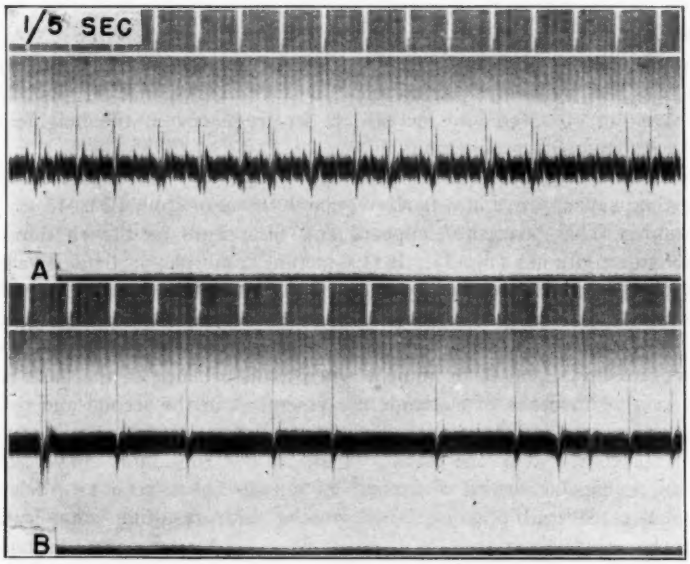

Fig. 3.—*A*, discharge of two normal units of the brachioradialis muscle of a patient with progressive muscular atrophy; the larger unit has a delayed rapid fluctuation ("parasite") attached to each action current, or primary wave, except for the second and the two last.

B, later observation on the same muscle, showing a large unit beginning a discharge, with a large parasitic, secondary electrical artefact, repeated in smaller size in subsequent beats except for the fifth, ninth and tenth.

the applied tap momentarily determines almost absolute synchronism, as I first described it.

The proprioceptive mechanism, which normally has both excitatory and inhibitory factors, develops a kind of reverberating alternation from

17. Denny-Brown, D.: On Inhibition as a Reflex Accompaniment of the Tendon Jerk and of Other Forms of Active Muscular Response, Proc. Roy. Soc., London. s.B **103**:321-336, 1928; footnote 6 *b*.

excitation to inhibition in the spastic state. Clonus is the result of this and is conditioned usually by factors raising the excitability of the spinal center. An interesting exception is the clonic rhythm found in some cases of advanced myopathy (fig. 10 *C*), suggesting that the

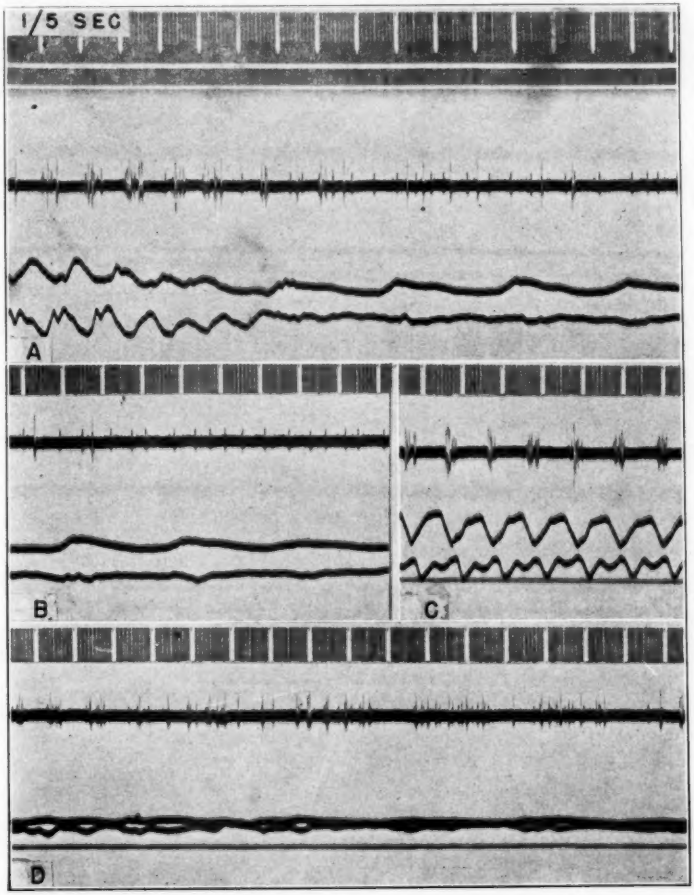

Fig. 4.—*A*, electromyogram from the biceps muscle in a case of idiopathic paralysis agitans. The lowest tracing is from a balloon over the same muscle and rises with contraction. The tracing above this is from a balloon over the flexor aspect of the wrist, showing a rise with each flexion of the wrist. The records show tremor at rest, subsiding spontaneously, with a transition to resting "rigidity."

B, a single unit making the transition from tremor rhythm to the regular discharge of rigidity.

C, fully developed tremor.

D, varying length of silent interval in the discharge of three units, as the rhythm changed spontaneously.

fundamental character of the "spastic" rhythm can also be related to disorder of the muscle. The electromyographic rhythm of spastic clonus (as opposed to the other phenomena of spasticity) is therefore

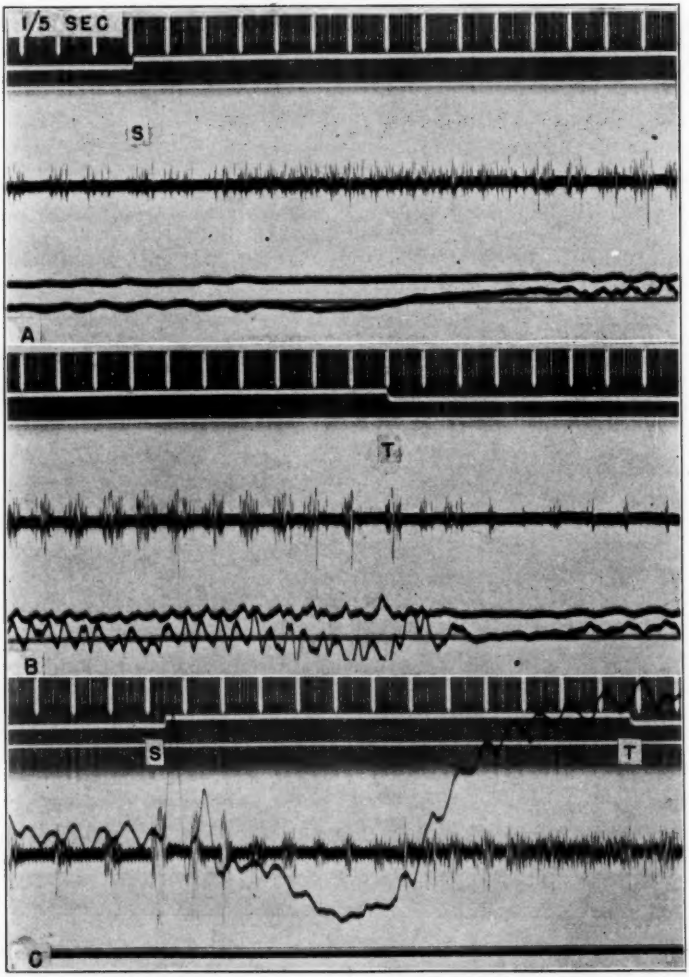

Fig. 5.—*A*, from the biceps muscle tracings from which appear in figure 4 (case of idiopathic paralysis agitans). At the signal mark above *S* the patient was instructed to flex the elbow gently.

B, continuation of the discharge in *A*. The patient was instructed to cease contracting at the signal mark *T*.

C, electromyogram from the extensor muscles of the wrist in a case of idiopathic paralysis agitans. Mechanical record from balloon in the hand. Between the signals *S* and *T* the patient was instructed to squeeze the balloon.

not considered specific for a disorder of the corticospinal neuronal connections. Its special characteristic is that the rhythm can be reset by a tap on the tendon, indicating that a heightened proprioceptor reflex activity is the source of the rhythmic interplay of excitation and inhibition.

Relative synchronism can also be determined by a disorder of extrapyramidal mechanisms. The electromyogram then differs from the clonus of spasticity. The most striking example of this class of disorders is parkinsonian tremor. Cobb,[18] Pritchard,[4] Ingebrightsen,[19] Schwab and Cobb [20] and Hoefer and Putnam [21] have drawn attention to the grouping of motoneuron discharges in parkinsonism. It has always impressed me, however, that here not only is each burst of discharge different from the last, but the wave formation of each burst differs in every beat. The same small group of units can often be followed through transitions from an irregular, haphazard discharge (rigidity) to a rhythmic grouping consisting of from one to four beats from each unit, separated by silences from the next burst (fig. 4). The sequence in each burst varies. When the tremor is fully developed, it is not the formation of the wave burst that is characteristic, but the appearance of regular gaps between them (fig. 4 *C*). These gaps are of either relative or absolute freedom of activity, but their progressive development suggests the rhythmic periodic blocking or inhibition of the center. Normal "background" discharge becomes more intense but is otherwise unchanged as it emerges from each silent phase.

In paralysis agitans there is an inherent disequilibrium of discharge such that at each new intensity the gaps are filled by a continuous increment (fig. 5 *A*), but if the discharge continues long enough the inhibitory gaps break through the increment (fig. 5 *B*). The tremor is then reasserted in the whole discharge again. Our records indicate that there is a hidden background of accumulating inhibition during any voluntary movement. Thus, if a voluntary increment is brief, the gaps are filled; but there is a sudden stop on cessation of effort, and then a burst of rebound (fig. 6 *A* and *B*).

The process of sudden cessation, followed by intense rebound after an inhibitory interval, can be reproduced by an artificial conflict between

18. Cobb, S.: Electromyographic Studies of Paralysis Agitans, Arch. Neurol. & Psychiat. **8**:247-264 (Sept.) 1922.

19. Ingebrightsen, B.: Practical Application of Electromyography in Diagnosis of Tremor, Acta psychiat. et neurol. **13**:11-20, 1938.

20. Schwab, R. S., and Cobb, S.: Simultaneous Electromyograms and Electroencephalograms in Paralysis Agitans, J. Neurophysiol. **2**:36-41, 1939.

21. Hoefer, P. F. A., and Putnam, T. J.: Action Potentials of Muscles in Rigidity and Tremor, Arch. Neurol. & Psychiat. **43**:704-725 (April) 1940.

excitation and inhibition in spinal reflexes in the experimental animal.[22] It is as though the excitation were driven through an accumulating resistance of inhibition, which is rhythmically reasserted as soon as the excitation is over. A physical analogy would be a blast of air blown through a door which has a closing spring. When the pressure of the blast lessens, the door is closed suddenly by the spring but rebounds rhythmically to allow further brief blasts of air. Also, in physical terms, the movements of the door could be "damped" in greater or less degree according to the proportion of resistance offered to the actuating pres-

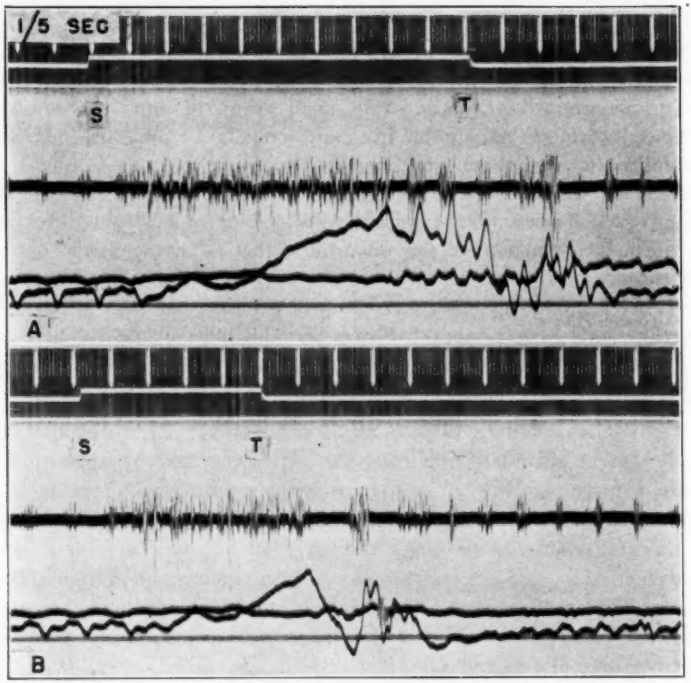

Fig. 6.—*A*, continuation of the discharge from the biceps muscle shown in figure 5 *A* (case of idiopathic paralysis agitans), showing result of brief voluntary contraction in the period shown by the movement of the signal line from *S* to *T*.

B, effect of a briefer contraction of approximately the same intensity.

22. Sherrington, C. S.: Reflex Inhibition as a Factor in the Co-Ordination of Movements and Postures, Quart. J. Exper. Physiol. **6**:251-310, 1913. Fulton, J. F., and Liddell, E. G. T.: Observations on Ipsilateral Contraction and Inhibitory Rhythm, Proc. Roy. Soc., London, s.B **98**:214-227, 1925. Creed, R. S.; Denny-Brown, D.; Eccles, J. C.; Liddell, E. G. T., and Sherrington, C. S.: Reflex Activity of the Spinal Cord, New York, Oxford University Press, 1932.

sure. Parkinsonian motor excitation is, in this physical sense, highly damped. The process of accumulating rebound can be seen in all grades of intensity in all types of activity (voluntary, synergic and reflex) in this condition. The rhythm is not identical throughout the musculature, but only relatively so, and a relative reciprocal relation is preserved.

The process of inhibitory conflict, as evidenced by abrupt electrical silences followed by abrupt and intense discharge, is also seen in epileptic clonic after-discharge, though the intervals of inhibitory damping are relatively longer.[23] In a slightly different sense, the same is true of cerebellar tremor, though the onset of each dampened place is here less abrupt and the block is more complete just as the inhibitory phase ends, leading to the sudden rebound of discharge, which then gives the tremor its jerkiness. From this point of view, parkinsonian and cerebellar tremor must be considered the result of the same general circumstance. In each, an excitatory process battles against an inhibitory counterpart of high intensity. The clinical differences between them are, in the last analysis, quantitative rather than qualitative. In parkinsonian tremor an added voluntary movement fills in the gaps by emphasizing the excitatory side of the conflict, whereas in cerebellar tremor a voluntary movement first intensifies the inhibitory aspect, thus stressing the tremor interval. But the parkinsonian muscle occasionally also shows a preliminary emphasis on existent tremor just as an added movement begins (fig. 5 *C*). Further observation of the inhibitory process, and close correlation of its behavior with anatomic studies, promise to be fruitful. Electromyographic study alone obviously cannot identify the source of origin of the disordered processes, or as yet more than approximately measure their quantity.

"Voluntary" Contraction.—Whereas the various tremors each have distinguishing characteristics that are sometimes useful in clinical differentiation, there is as yet no other electromyographic criterion to show whence a particular muscular spasm or contraction is derived. I can say that a particular electromyographic tracing has the characteristics of spastic clonus, or of parkinsonian tremor, or of a slower type of tremor. But automatic, presumably reflex, contractions associated with pain have an appearance indistinguishable from willed contraction of muscles. If infiltration of muscle with procaine abolishes the automatic response, leaving willed contraction still possible, the question whether the original contraction was reflex or of some other type is

23. Cooper, S., and Denny-Brown, D.: Responses to Stimulation of the Motor Area of the Cerebral Cortex, Proc. Roy. Soc., London, s.B **102**:222-236, 1927. Denny-Brown, D., and Robertson, E. G.: Observations on Records of Local Epileptic Convulsions, J. Neurol. & Psychopath. **15**:97-136, 1934.

still undecided, for its associated pain is also lessened. The continuation of such spasms with degrees of attempted relaxation which abolish all discharge in the normal control proves only that relaxation is difficult. In this category can be included a series of different types of continued electromyographic activity, such as that in the muscles around an acutely painful joint, those related to various types of painful spasm of the back [24] and that frequently encountered in the tender muscles of poliomyelitis and polyneuritis.[25] I classify these as "painful spasm."

It is well established as a result of the observations of Smith,[1c] Lindsley,[1d] Seyffarth [16] and others, including Pennybacker and myself [2] that the same motor units regularly initiate discharge when a willed contraction is repeated. The motor units are "recruited" one by one to join the discharge, and Seyffarth [16] has plotted the rapid increase in rate of discharge for each of several units as it joins the group. A relative order of discharge of motor neurons is preserved. Do these same motor units serve other functions, or, on the other hand, are different motor units set aside for postural reflexes, for spasticity and for extrapyramidal rigidity? The question is complicated by the fact that motor weakness most commonly accompanies spasticity, so that *ipso facto* some units are removed from normal voluntary control, and discharge of the others solely in reflex function does not then indicate a natural independence. It has already been stated that voluntary discharge becomes involved in parkinsonian tremor. It is difficult to be sure that a given unit which is active in parkinsonian rigidity is not also involved in the late phases of voluntary movement, when individual rhythms are obscured.

The question may be approached in a different way. There are different degrees of availability of motor units for a discharge in response to willed effort. In the course of studies of the contraction of synergic and fixing muscles, I have found features that appear regularly to distinguish the use of a muscle as a prime mover in Beevor's [26] sense from that which distinguishes its use as a fixator, or synergist, for some other prime mover. As Duchenne,[27] Beevor [26] and others

24. Buchthal, F., and Clemmesen, S.: On the Differentiation of Palpable Muscle Affections by Electromyography, Acta med. Scandinav. **105**:48-66, 1940.

25. Schwartz, R. P., and Bouman, H. D.: Muscle Spasm in the Acute Stage of Infantile Paralysis as Indicated by Recorded Action Current Potentials, J. A. M. A. **119**:923-926 (July 18) 1942. Schwartz, R. P.; Bouman, H. P., and Smith, W. K.: The Significance of Muscle Spasm in the Acute Stage of Infantile Paralysis Based on Action Current Records, ibid. **126**:695-702 (Nov. 11) 1944. Watkins, Brazier and Schwab.[13] Brazier, Watkins and Schwab.[14]

26. Beevor, C. E.: The Croonian Lectures on Muscular Movements and Their Representation in the Central Nervous System, London, Adlard & Son, 1904.

27. Duchenne de Boulogne, G. B.: Physiologie des mouvements, Paris, J. B. Baillière & Fils, 1867.

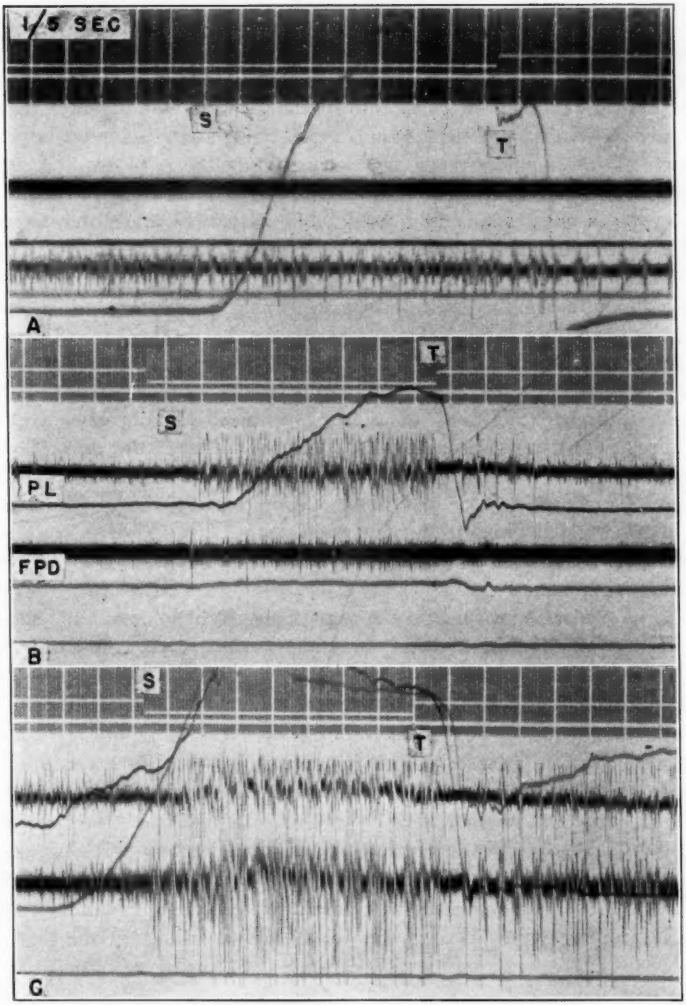

Fig. 7.—*A*, electromyogram from the palmaris longus muscle of a normal subject. The moving line tracing is from a balloon held in the palm. The record begins during a voluntary flexion of the wrist. From *S* to *T* the subject was instructed to grasp firmly, keeping the wrist flexed. At *T* he relaxed the grasp and began to extend the wrist.

B, tracings from a normal subject. The upper oscillographic tracing is from the flexor palmaris longus muscle; the lower is from the flexor profundus digitorum. The upper line tracing (*PL*) is from a balloon over the tendon of the palmaris longus muscle, showing a rise when that muscle contracts; the lower line tracing (*FPD*) is from a balloon in the hand and records flexion of the fingers. In the signaled interval (*S* to *T*) the subject voluntarily flexed the wrist.

C, continuation of the discharge shown in *B*. The record begins during increasing flexion of the wrist, to which is added a strong flexion of the fingers during the interval *S* to *T*.

have shown, individual muscles are used in different ways in different movements. Careful observation of the units shows that the fixity of the first set of units to come into discharge in a willed contraction is related only to that particular contraction. Seyffarth [16] showed not only that there are separate pools of units first activated in biceps brachii for flexion of the elbow and for supination, but that in a combined movement yet a third set is first used. My associates and I have found that the set of units in the flexor profundus digitorum first to begin discharge in the contraction of grasping is different from those beginning discharge in the same muscle in flexion of the wrist. Different groups of units in the flexor carpi ulnaris begin the three types of contraction—flexion of the wrist, ulnar deviation of the wrist and the movement of grasping (fig. 7 *A*). Further, we have observed that the type of discharge differs. The usual confused asynchronous shower of direct willed innervation occurs when the muscle is the prime mover and is directly producing the movement desired, as in the palmaris longus in figure 7 *B* or the flexor profundus digitorum (lower) in figure 7 *C*. If the muscle then functions as a fixator, so that it is used, for example, to fix the posture of the wrist during voluntary flexion of the fingers, the type of discharge is periodic or clonic (fig. 7 *B* and *C*). In control experiments for a previous study of myotonic grasp, Nevin and I [28] found that for most movements except direct flexion of the wrist the discharge of the palmaris longus muscle was of grouped clonic type. It is chiefly a fixator for movements of the hand.

The study of dystrophia myotonica by Nevin and myself [28] indicated that in this disease, at a stage when only the intrinsic muscles of the hand and tongue showed percussion myotonia, the delay in relaxation of grasp was related to a central reflex effect from the myotonic muscles. Thus the flexor carpi ulnaris showed striking myotonic delay in relaxation after voluntary grasping and none after ulnar deviation of the wrist. This indicated that a central reflex effect, taking origin in the proprioceptive fibers of the prime mover, influenced the fixating muscles. The effect appears to take place both during and immediately after the movement. In normal muscle acting as prime mover the discharge ceases abruptly immediately the subject is told to relax. After a brief interval of about $\frac{1}{10}$ second, rhythmic clonic bursts of discharge appear, gradually becoming less synchronized (fig. 7). From experiments conducted by Nevin and myself on our own limbs, we were satisfied that this abrupt cessation and rhythmic rebound occurred both when there was simple, but immediate, relaxation to a resting and unsupported posture and when the antagonist was directly innervated.

28. Denny-Brown, D., and Nevin, S.: The Phenomenon of Myotonia, Brain **64**:1-18, 1941.

The sudden silence, followed by rhythmic rebound activity, is identical with experimental spinal "rebound" when an excitatory reflex has been provoked against a background of inhibition. It appears legitimate to assume that the presence of conflicting excitation and inhibition in fixation is part of a willed movement. Our experiments on dystrophia myotonica suggest that one or both of the conflicting elements come from the prime mover.

In progressive spastic paraplegia and quadriplegia the increasing intensity and prominence of the rhythmic rebounds immediately following a voluntary movement is an early sign of the disorder of willed movement by the spastic process (fig. 8 *A*). Later, the spastic grouping carries through into the voluntary discharge (fig. 8 *B*). More highly integrated postural reactions, such as the grasp reflex and tonic innervation, also show grouped discharge of more irregular type, bespeaking less direct cross currents of conflicting effects (fig. 8 *C*).

The motor units involved in synergic contraction are so commonly much larger than those involved in the early stages of willed primary movement that this can be no mere accident of needle placement. On the other hand, a small unit may occasionally be found to serve both functions, and in intense discharge of both types the same large units in the same parts of the muscle may take part. Thus it is clear that voluntary control of a muscle may use the same units for different purposes, but the effects begin regularly in different groups of neurons.

The electromyogram of spastic muscles in cases of spastic paraplegia is identical in appearance with that of decerebrate rigidity; furthermore, the muscles earliest and most intensely affected are the deep heads of extensors in the lower limbs (a deep portion of the vastus medialis, crureus and soleus), as they are in the decerebrate animal. These muscles in man are also active in maintaining posture in the normal process of standing, but the discharge is slight when the leg is held straight. In man, straightness of the lower limb is favored by purely physical factors at the knee joint, and in normal circumstances muscular effort is minimal in this posture. The larger part of the vastus muscles and double joint muscles, such as the rectus femoris and the gastrocnemius, are usually entirely inactive in these circumstances, but it is not correct to interpret their myogram during rest as indicating that no discharge at all is necessary for standing posture in man. The small corrections and tensions necessary to maintain posture will be found in the soleus and crureus and in the shorter, darker, head of the vastus medialis, just as the minimal tendon jerk will be found in the same muscles. This distribution indicates that normal posture is based on the stretch reflex, but the proof of absolute identity would be difficult. The question of "tone" of a completely relaxed, supported limb is a different matter and will be discused later.

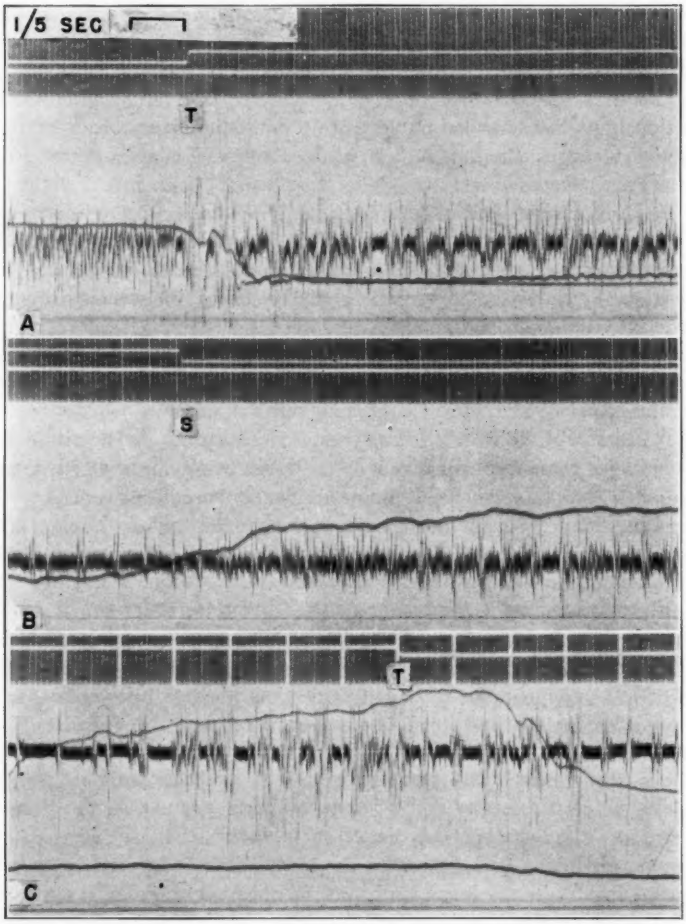

Fig. 8.—*A*, electromyogram from the flexor profundus digitorum muscle in a case of spastic hemiplegia (of six months' duration), showing postural rebound. The mechanical tracing shows tightening of the tendon of the muscle as it contracts. The figure begins during a voluntary grasp, which ceases at the signal at *T*, after which the muscles return to spasticity. A balloon in the palm gives a second mechanical tracing, which comes on the record at *T*, as the grasp was relaxed.

B, electromyogram and tracing from the vastus medialis muscle in a case of spastic paraplegia, showing clonic grouping of units before contraction and emergence of clonic rhythm as contraction proceeds. Voluntary extension of knee began at *S*.

C, electromyogram from the flexor profundus digitorum muscle with mechanical tracing from the whole flexor group, showing clonic rhythm during tonic innervation, in a patient with a tumor of the frontal lobe. The patient was beginning a voluntary grasp at the left of the figure and was instructed to relax at *T*.

In spastic spinal paraplegia in man the effects of local reflexes, causing reflex excitation and inhibition, are easily shown. In particular, the stretch reflex with lengthening and shortening reactions, the knee jerk, the silent period that follows it and spinal clonus have the same characteristics as those my colleagues and I have observed in chronic spinal animal preparations. It is possible to study the tendon jerk and silent period in one human motor unit in man. In mild tetanus in man all these reflex effects can be studied with great facility (fig. 9), evidently owing to enhancement of the excitatory processes of the spinal reflex by tetanus toxin. In both these instances it is remarkable how readily postural discharge can be inhibited, so that the galvanometer tracing becomes absolutely still in the silent period and during a nociceptive flexor reflex.

When the background is mild voluntary contraction, the silent period of the tendon jerk is extremely brief, or altogether absent. In conditions of spastic weakness due to cerebral lesions, the ease with which the silent period can be demonstrated is roughly proportional to the degree of paralysis. We view this difference as further evidence that willed contraction innervates primarily different units from those involved in the spinal stretch reflexes, and that such units are relatively less amenable to spinal inhibitory processes. That the difference is relative, rather than absolute, is seen in the manifest ability of strong willed contraction to involve the soleus muscle, which can be observed on the outer aspect of the leg in thin persons. Further, in spinal spasticity without muscular weakness, voluntary contraction can be observed, both by eye and by electromyogram, to begin in the lower vastus medialis and soleus, where the tendon jerk and stretch reflex normally reside. In mild tetanus the same units discharge first in willed movement, ipsilateral reflex and stretch reflex (fig. 9 *A, B* and *C*), as though heightened reflex excitability had lowered their threshold to voluntary as well as reflex contraction. It is concluded that any segregation of motor units for different purposes is relative and quantitative. It is not believed that there is any fundamental difference in types of discharge between willed contraction and postural activity that cannot be explained in terms of the greater intensity of excitation of the former. Thus, postural activity in human muscle, as was long since shown in the experimental animal,[6b] increases by recruitment of fresh units at low maximum rates of discharge (5 to 10 a second), as compared with increase both by recruitment and by discharge frequency in willed movement.[29] The resistance of voluntary contraction to spinal inhibition probably results from similar overwhelming excitatory effect. Similarly, the cocontraction of antagonists by voluntary fixation indi-

29. Lindsley.[5] Seyffarth.[16]

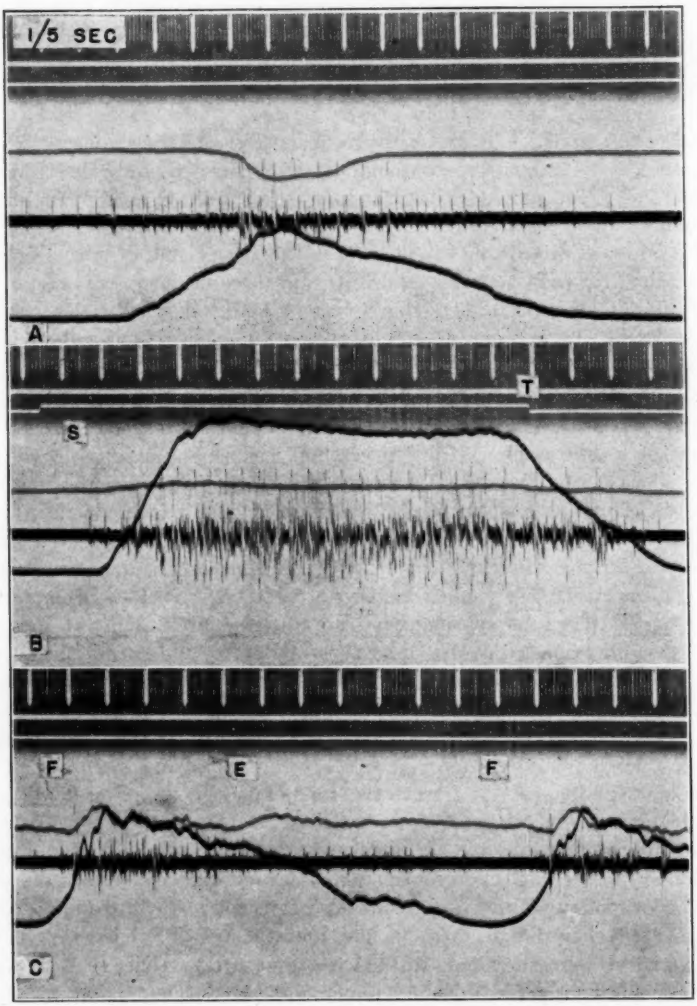

Fig. 9.—*A*, electromyogram from the most distal and deepest part of the vastus lateralis muscle in a patient with mild tetanus from an infected wound. Trismus with generalized slight rigidity of the abdomen was present. The upper (mechanical) tracing is from a balloon attached to the great toe, showing a rise with dorsal flexion of the toe. The lower (darker) tracing shows contraction of the quadriceps (balloon over vastus lateralis). The response shown, extension of the hip, knee and ankle with plantar flexion of toes (ipsilateral extension reflex) was provoked by a scratch of the sole of the foot.

B, continuation of discharge shown in *A*, showing voluntary extension of the knee.

C, showing the effect of passive flexion (*F* to *E*), followed by passive extension (*EF*) of the knee.

cates the driving power of willed effort, though the rhythmic clonic conflict seen in the electromyogram probably represents in part the antagonism of spinal reciprocal relationships. Beevor [26] well illustrated the fixity, as well as the driving power, of willed movement synergies in demonstrating the difficulty in flexing the wrist while a strong grasp is made. Finally, lest it be assumed too readily that willed contraction is directly comparable to the effect of stimulation of the motor area of the cortex, reference may again be made to the conflict between willed movement and the jacksonian epileptic discharge. In this circumstance, muscle synergies immediately vanish and are replaced by an even more powerful cocontraction of antagonists. The existence of powerful inhibitory undercurrents is then shown by the intense rebound contractions of postepileptic clonus. These are also found in post-stimulation epilepsy in the experimental animal.[23] Intentional movement is gravely disordered in the experimental animal by deafferentation, whereas movement induced by cortical stimulation is unaffected.[30] There is evidence, therefore, that the synergies and fixations incidental to willed contraction are derived from fixed patterns of excitation that override the reflexes from proprioceptive fibers, both of the prime mover and of the synergically acting muscles, and that the "clonic" electromyographic record reflects the balance of antagonisms involved.

Fatigue of Voluntary Contraction.—In purely muscular disorders, such as pseudohypertrophic muscular dystrophy, the electromyogram of voluntary contraction reveals a large number of very small motor units discharging at natural rates. This change is obviously attributable to the reduction in number of muscle fibers per unit and to the relative increase in connective tissue. My colleagues and I have found in several patients an additional change, which is shown in figure 10 *A* and *B*. Here, although willed effect is maintained, the muscular contraction is steadily declining, and the electromyogram shows the late appearance of isolated, but repeated, large excursions of sufficiently regular shape to enable the inference that larger units are now taking part. For the remainder of the record such units alternately appear and disappear. The same phenomenon also occurs in our records of progressive failure of contraction in cases of myasthenia gravis and in cases of normal fatigue. In myasthenia gravis we have seldom observed the characteristic changes in amplitude of the beats of a single unit observed by Lindsley,[31] whereas sudden cessation of discharge of a unit, as noted by others in normal fatigue,[16] is a common occurrence. Changes in size [16] and in shape [11] of the action current observed with

30. Sherrington, C. S.: Quantitative Management of Contraction in Lowest Level Coordination: Hughlings Jackson Lecture, Brain **54**:1-28, 1931.

31. Lindsley, D. B.: Myographic and Electromyographic Studies of Myasthenia Gravis, Brain **58**:470-482, 1935.

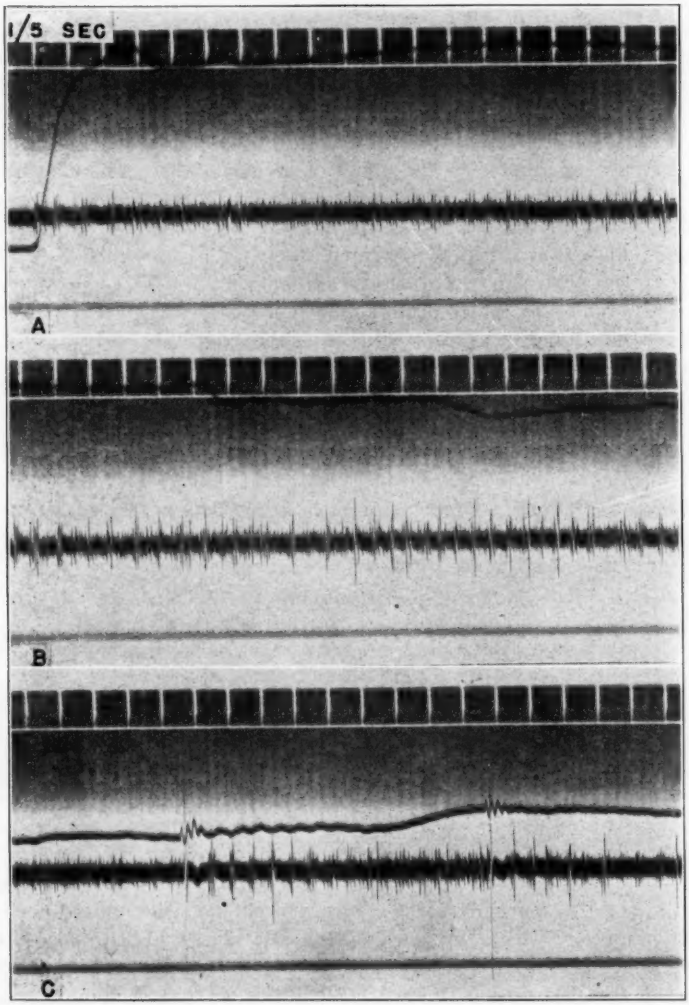

Fig. 10.—*A*, electromyogram from the internal head of the gastrocnemius in a case of familial pseudohypertrophic muscular dystrophy. The mechanical myogram is from a balloon placed between the sole of the foot and the stirrup board attached to the flexed knee by a loop of adhesive tape, thus recording the power of plantar flexion of the ankle. The patient began plantar flexion in response to a request for maximal effort.

B, continuation of the contraction shown in *A*, showing the appearance of larger units as the contraction tension declined. These larger units could be observed to disappear and reappear for two to ten beats at intervals during ten minutes of gradually declining contraction.

C, two tendon jerks in the same muscle.

needle electrodes are always open to suspicion of movement of the needle in relation to the contracting fibers as the contraction proceeds. When, as a result of prolonged contraction, large units reappear in the rhythm, and it is reasonably certain that the needle electrode is not slipping in the muscle, it is concluded that the patient or subject is attempting to ease the burden of fatigue by changing the nature of the contraction. It has already been mentioned that most muscles can be contracted voluntarily in two or more ways, and we interpret the change in type of units as evidence that one movement has been substituted for another. In support of this conclusion is the frequent observation that, in response to an exhortation to supreme effort, a set of units which has ceased to discharge will again appear in the record in the natural rhythm of discharge. Such observations warn that, whatever the nature of subjective fatigue, the motor unit discharge must be carefully controlled if correct deductions are to be drawn from the failure of innervation. This phenomenon of alternation of discharge is the only kind of relief from fatigue by rotation of activity of units that we have observed.

Hypotonia.—Though the clonic rhythm of spasticity and the increased tendon jerk give evidence that exaggeration of the stretch reflex is the essential mechanism of that condition, it is more difficult in man to find reliable criteria of the presence of the stretch reflex in normal degrees of posture. It is not possible to isolate a muscle center from all stimuli except stretch of the muscle concerned. Only the distribution of the discharge in relation to the low threshold units for the tendon jerk is available for analysis. On such evidence, it appears that the least motivated postures are indeed responses in the stretch reflex mechanism.

The question then arises as to the nature of firmness of muscle in the normal subject when the limb is not subjected to maintenance of bodily posture. I agree with many observers that in the completely relaxed and supported muscle there are no action potentials.[32] Magun [33] used Schaltenbrand's apparatus to compare the purely elastic properties of resting normal human muscles with those of the same muscles paralyzed by intrathecal anesthesia and found no difference. In the supported relaxed normal limb the muscles are flaccid and the tendons loose, and it is not conceivable that any contractile activity exists. The muscles of the calf can readily be brought into such a state in most persons.

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32. Lindsley, D. B.: Characteristics of Single Motor Unit Responses in Human Muscles During Various Degrees of Contraction, Am. J. Physiol. **113**:88-89, 1935; ibid.[5] Hoefer, P. F. A.: Innervation and Tonus of Striated Muscle in Man, Arch. Neurol. & Psychiat. **46**:947-972 (Dec.) 1941.

33. Magun, R.: Lassen sich in der gut entspannten Muskulatur des Menschen myotatische Reflexe nachweisen? Arch. f. d. ges. Physiol. **243**:603-610, 1940.

By the term hypotonia the clinician means a looseness of muscle and joint that is appreciable, not in the relaxed, supported limb, but in the limb that is maintaining a posture (outstretched hands) or is involved in movement (loose-jointed gait). It is, therefore, not surprising that in the presence of profound cerebellar hypotonia, manifested by ease of displacement of the outstretched limbs on the affected side, and by pendular swinging of the dependent, unsupported leg after a tendon jerk or other movement, some action potentials are in our experience still recordable from the deep postural muscles during the stretching phase of larger passive swinging movements. The stretch reflex muscles are still active in this condition, but less active than normally.

Hypotonia in the clinical sense, therefore, takes no account of the consistency of muscle to palpation. The clinician includes flabbiness or softness in consistency in the term "flaccidity," but his essential criterion is lack of resistance to passive stretch. An atrophic flaccid muscle paralyzed by a lesion of the lower motor neuron is certainly softer than normal, and the extremes of movement at the corresponding joint commonly show a less elastic resistance. In our view, this is not hypotonia in the usual clinical sense, but is a separate property, the other extreme of which is the state of being "muscle bound" exhibited after muscular training in certain types of slow exertion. It appears to correlate with size of muscle, and, hence, with size of muscle fiber. It has not a direct relation to the presence or degree of postural reflex activity in animals, and in clinical states it may be expected to be increased only when intense and persistent muscular activity has secondarily induced hypertrophy of muscle, as in athetoid states. Such changes in consistency cannot be expected to have any electromyographic index. The electromyogram may therefore be expected to give indication of all other nervous and adaptable postural activity, though the methods of grading such activity at present available allow only very coarse quantitation.

CONCLUSIONS

Electromyography has valuable clinical uses and is a profitable field for further study. When used as an indicator of the neuronal activity in disease processes, it should be controlled by critical appraisal of the mechanical contractile activity in the muscle concerned, for the electrical field of motor units is large and grows more extensive in proportion to the intensity of discharge. Spread of rhythms to two or more sets of leads is particularly liable to occur from large units, particularly in atrophic muscle. Few types of change are specific for types of nervous disorder, and the physiologic reasons for this are discussed.

Boston City Hospital.

SPASMODIC TORTICOLLIS

I. Physiologic Analysis of Involuntary Motor Activity

ERNST HERZ, M.D.
AND
PAUL F. A. HOEFER, M.D.
NEW YORK

SPASMODIC torticollis is clinically defined as abnormal involuntary innervation of muscles of the neck resulting in more or less sustained movements or in deviation from the normal of the posture of the head. Both types of motor abnormality may be present in the same case.

Compensatory movements in certain types of oculomotor and vestibular disorders, as well as structural abnormalities of muscles or bones of the neck, may cause a change in the normal position of the head. Neither, however, is the result of abnormal involuntary activity, as is spasmodic torticollis, to which entity this study is limited.

Forty-three patients with spasmodic torticollis were seen at the Neurological Institute of New York between 1930 and 1944. A clinical analysis of the neurologic and psychiatric observations in this group and an evaluation of the results of various forms of operative treatment in 18 of them will be published separately.

In the present report, an attempt is being made to analyze more closely than by mere clinical inspection the mechanism, pattern and distribution of the abnormal involuntary motor activity of torticollis, especially in relation to other forms of dyskinesia, such as that seen in athetosis, dystonia and paralysis agitans. For this purpose, muscle action potentials were recorded from the muscles obviously involved, as well as from others on the same and on the opposite side of the neck, trunk and upper extremity showing clinically little or no participation in the abnormal activity. In addition, the pattern of the hyperkinesis was analyzed with moving pictures. Both methods have been used

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From the Department of Neurology, Columbia University College of Physicians and Surgeons, and the Neurological Institute of New York.

in earlier investigations [1] concerned with normal and abnormal movement in man. Some of the earlier findings are pertinent to the present study and are summarized here.

(*a*) Normal intact muscle at rest, i.e., muscle not employed in any form of movement or in the maintenance of posture, shows no signs of being under innervation, and no action potentials are recorded in tracings from such muscle.

(*b*) With the onset of volitional or reflex innervation, action potentials appear in the record from activated muscle roughly in proportion to the strength of contraction.

(*c*) During simple voluntary movement antagonist muscles relax in keeping with Sherrington's "law of reciprocal innervation." No electrical activity is found in these muscles.

(*d*) On the other hand, resistance to passive movement is a reflex contraction in response to stretch. This reflex contraction is regulated by the briskness of the stretch and the degree to which the muscle is stretched; it is also accompanied with action potentials, again roughly in proportion to the strength of the contraction. The stretch response is increased in conditions such as spasticity and rigidity. In these two conditions active voluntary innervation may lead to passive stretching of the antagonist muscles and may elicit a stretch response, which, in turn, detracts from the power available for the intended movement.

(*e*) During alternating tremor in paralysis agitans rhythmic bursts of highly synchronized action potential groups are recorded at the rate of the alternating movement. They are so timed that they coincide with the active movement; little or no activity is recorded between the bursts.

(*f*) Irregular simultaneous innervation of antagonists is seen in the records of pateints with athetosis. More or less sustained activity may change abruptly in intensity and may be interrupted by bursts of rhythmic activity. Both forms of innervation are found to be present simultaneously in different parts of the same muscle especially when needle electrodes are used for recording from fairly localized areas.

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1. (*a*) Hoefer, P. F. H., and Putnam, T. J.: Action Potentials of Muscles in Normal Subjects, Arch. Neurol. & Psychiat. **42**:201 (Aug.) 1939; (*b*) Action Potentials of Muscles in Rigidity and Tremor, ibid. **43**:704 (April) 1940; (*c*) Action Potentials in Athetosis and Sydenham's Chorea, ibid. **44**:517 (Sept.) 1940. (*d*) Hoefer, P. F. H.: Innervation and Tonus of Striated Muscle in Man, ibid. **46**:947 (Dec.) 1941. (*e*) Herz, E.: Die amyostatischen Unruheerscheinungen, Leipzig, Johann Ambrosius Barth, 1931; (*f*) Dystonia: I. Historical Review; Analysis of Dystonic Symptoms and Physiologic Mechanisms Involved, Arch. Neurol. & Psychiat. **51**:305 (April) 1944.

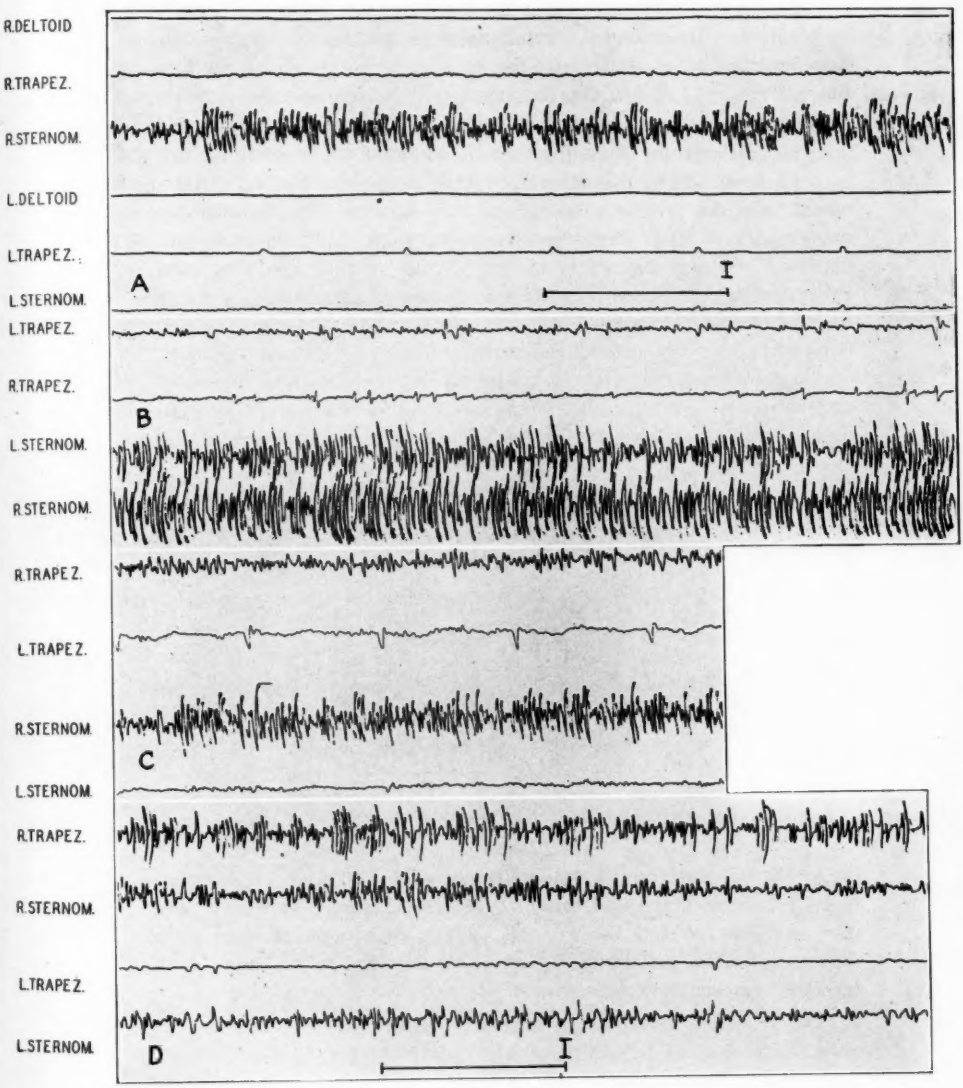

Fig. 1.—Electromyographic records with variations of pattern in a case of torticollis. Calibration equals 200 microvolts; time, 1 second. *A*, maximum of sustained activity in the right sternocleidomastoid muscle; *B*, prevalent sustained activity of both sternocleidomastoid muscles; *C*, sustained activity confined to the right side, the sternocleidomastoid being more affected than the trapezius; *D*, sustained activity of both the sternocleidomastoid and the trapezius of the right side and the sternocleidomastoid of the left side.

(*g*) Dystonic movements and postures are maintained similarly by constant, often maximal, simultaneous contractions of large groups of muscles, usually of the trunk, the neck and the proximal portions of the extremities. When this contraction is maintained, as it often is, the appearance of a motor performance is usually abolished.

The methods for recording action potentials of striated muscle in man as developed in this laboratory have been described in detail elsewhere.[1a] In the present investigation only surface leads were obtained, using pairs of disk electrodes, made of solder and about 1 cm. in diameter. A six channel Grass ink-writing oscillograph was used as the recording instrument. Surface leads permit a recording of the gross total of impulses arising from a muscle and, properly placed, do not pick up activity from neighboring muscles. With the ink-writing oscillograph, records from as many as six muscles can be obtained simultaneously. The upper frequency limit of the recording pens is only about 90 cycles per second. This high inertia causes marked

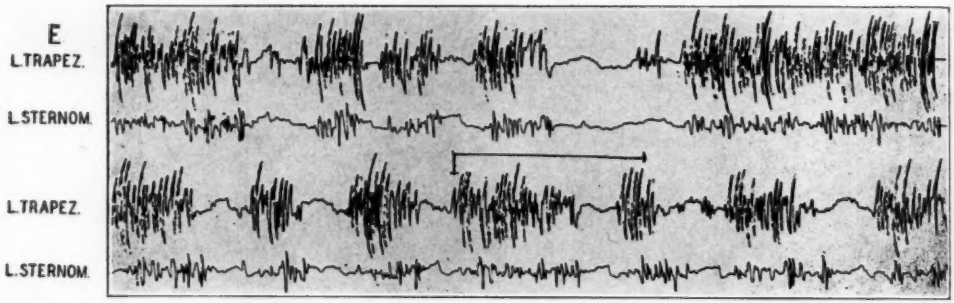

Fig. 2.—Shorter and longer groups of spike potentials. Calibration equals 200 microvolts; time, 1 second.

distortion of single spike potentials, as well as loss of resolution of high frequency volleys of spikes. However, single spikes at a low rate of discharge and the over-all pattern of groups of impulses are well recognizable, as shown by comparison with records taken with a cathode ray oscillograph.[1a]

The abnormal movement in torticollis may vary in its clinical appearance, as stated at the beginning of this report. In most instances, however, a single dominant feature tends to obscure the fact that the movement is more complex and in practically all our cases involved both sides of the neck. This is brought out by electromyographic records, a number of which are presented in figures 1 and 2.

The involuntary contraction is mostly sustained and leads to a slow turning or twisting of the head, usually to one side or, in some

instances, forward or backward. The terminal position of the head is usually held for a while before relaxation begins and in some instances is held for such long periods as to cause secondary postural changes. Several examples of this form of torticollis are shown in figure 1, *A* to *D*.

Figure 1 *A* is a record from the deltoid, trapezius and sternocleidomastoid muscles on both sides. The maximum of activity in this case is found in the tracing from the right sternocleidomastoid muscle, where it was somewhat irregularly sustained. In addition, minimal traces of muscular activity are found in the tracings from the left sternocleido-

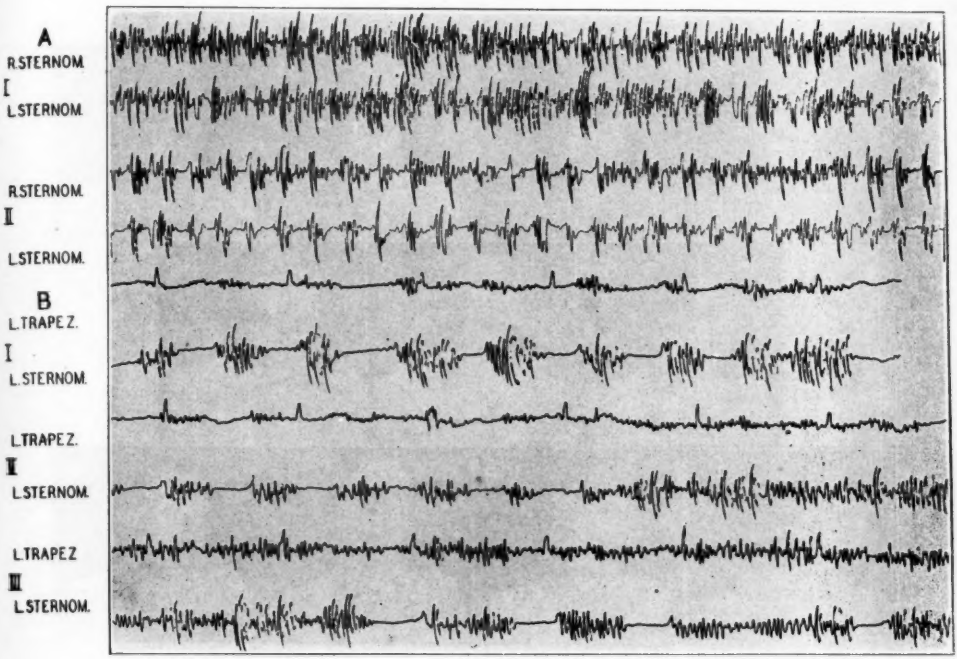

Fig. 3.—Electromyograms of rhythmic activity superimposed on sustained activity. Calibration equals 200 microvolts; time, 1 second.

A: I, sustained activity of both sternocleidomastoids; *II,* regular rhythmic activity in the same muscles.

B: I, irregularly spaced bursts; *II,* short bursts, followed by sustained activity; *III,* long-sustained activity of the trapezius and activity of longer and shorter duration in the sternocleidomastoid.

mastoid muscle. Figure 1 *B* shows sustained activity of somewhat irregular pattern and of near maximal amplitude in both sternocleidomastoid muscles, with a consistent slight preponderance of the right side. Slight, but definite, signs of activity are found in the two trapezius muscles. In this case the patient's head was held in opistho-

tonos, a position occasionally referred to as "retrocollis." Figure 1 *C*, again from the trapezius and sternocleidomastoid muscles on both sides, shows activity practically limited to the muscles on the right, with only minimal activity in groups of low voltage potentials seen on the left side. (In this case, as well as in the case shown in figure 1 *A*, an artefact due to the electrocardiogram can easily be identified.) In figure 1 *D* most of the activity is recorded from the right trapezius muscle, less from the right sternocleidomastoid and, again, less from the left sternocleidomastoid. The last component had not been recognized by clinical examination.

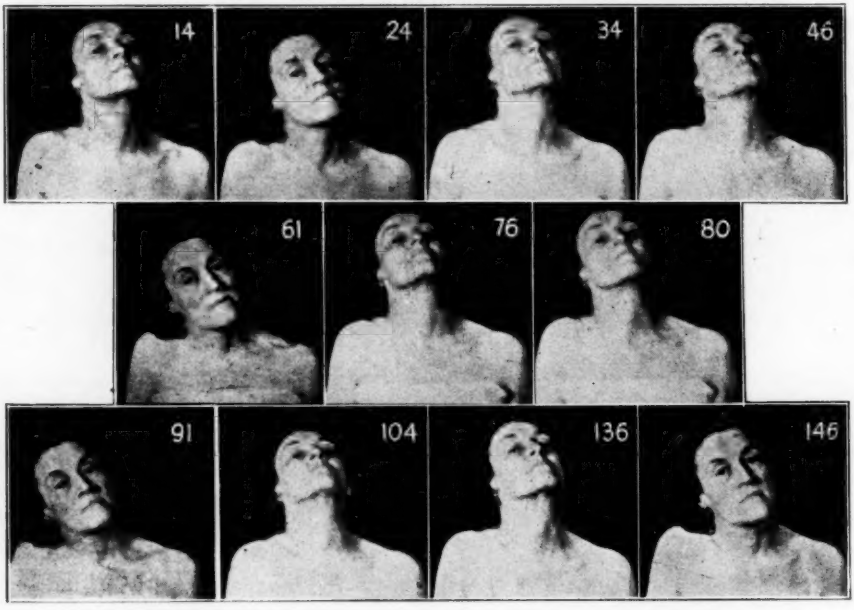

Fig. 4.—Irregular alternating activity (myorhythmia) in case whose record (*B*) is shown in figure 3. Frames are taken from slow motion pictures, showing the end positions (forward flexion and backward extension).

A different pattern of activity is noted in figure 2. In this case, as in others, muscles on both sides of the neck were found to be activated. However, a characteristic variant is seen in the tracings from the trapezius and the sternocleidomastoid muscles on the left. This part of the activity consists in recurrent groups of spike potentials of varying duration, and at times in an almost rhythmic pattern. Clinically slow-turning movements were noted, superimposed by jerking movements in all directions and at irregular intervals.

The next 2 cases present rhythmic activity. Figure 3 *A* consists of two tracings from 1 of these cases, with records obtained from both sternocleidomastoid muscles. In this case two types of movement were presented: one, a stiff turning of the head with a regular tremor superimposed; the other, a pure, regular tremor, which persisted even when the turning movement ceased. The electromyograms bear out the two clinical patterns of movement. The upper tracing shows sustained activity with distinct grouping of impulses, which were nevertheless continuous; the lower tracing is practically indistinguishable from the record of a parkinsonian alternating tremor at the rate of 6 per second.

Figure 3 *B* shows another variant of rhythmic movement. In this instance the clinical pattern was complicated, consisting of shaking, forward flexion and extension of the head, the terminal positions being maintained for varying periods. Three tracings are presented in this

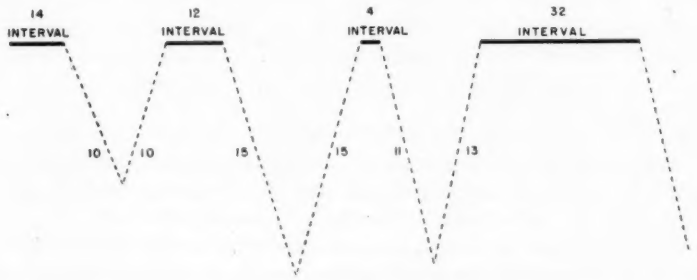

Fig. 5.—Time relations of alternating movements and free intervals.

case, representing records from the trapezius and sternocleidomastoid muscles on the left. The electrical activity is consistently higher in the record from the sternocleidomastoid muscle. It varies from irregularly spaced bursts with intervening inactive periods to irregularly sustained activity. Similar features are seen in the record from the trapezius, but in this muscle the sustained activity is more prominent than the rhythmic bursts. A moving picture analysis of the same case is presented in figure 4. The frames were enlarged and the time relations of movement and free interval periods were plotted in diagrammatic form (fig. 5). A full period of flexion and extension was considered a unit of movement, and counts of the frames show strikingly the irregularity of this component of movement in that it required 14, 12, 32, 4, and again 32, frames in successive "units." This irregular rhythmic form of movement has been termed "myorhythmia." [10]

COMMENT

The widespread bilateral involvement of muscles of the neck in spasmodic torticollis is not generally recognized, though it was well described by Walshe.[2] Action potential and moving picture studies show patterns of motor activity as described in specific forms of abnormal involuntary movements, though limited to the muscles of the neck, rather than generalized. Predominant are dystonic movements, slow and sustained, with the same characteristics as those described in dystonia musculorum deformans.[1f] Fast, jerking movements, resembling tic twitching or rhythmic activity, may be superimposed. In some cases the latter resembles typical alternating tremor, as seen in paralysis agitans; occasionally the alternating units follow each other irregularly, as in myorhythmia. In the clinical literature,[3] torticollis has been classified as "clonic," "tonic" and "tonic-clonic." This nomenclature, borrowed from other fields of clinical neurology, is misleading and should be abandoned in favor of terms referable to other forms of abnormal involuntary movements to which troticollis seems related. Similarly, the term "spasm" [4] would appear unfounded, as the physiologic mechanism for "spasm" is quite different from that of torticollis.

SUMMARY

The physiology of innervation of muscles in spasmodic torticollis was studied by means of action potential records of muscles on both sides of the neck and, in addition, by motion picture analysis.

Several types of involuntary motor activity were thus differentiated: (1) a predominantly dystonic pattern with sustained clinical and electromyographic activity; (2) quick, jerking movements at irregular intervals and of varying duration; (3) rhythmic activity occurring either alone or superimposed on dystonic activity.

In almost all cases muscles on both sides of the neck were found to be involved, and in most cases the physiologic pattern appears far more complicated than the clinical appearance.

It is suggested that the clinical distinction of "clonic," "tonic" and "tonic-clonic" torticollis and descriptive terms, such as "mobile spasm," be abandoned in favor of a nomenclature based on the similarity of movement patterns in torticollis to those in known forms of abnormal involuntary activity.

710 West One Hundred and Sixty-Eighth Street.

2. Walshe, F. M. R.: Diseases of the Nervous System, Baltimore, Williams & Wilkins Company, 1947.

3. Redard, P.: Le torticolis et son traitement, Paris, G. Carré & C. Naud, 1898. Barré, J. A.: Le torticolis spasmodique, Rev. neurol. **36**:985, 1929. Cruchet, R.: Traité des torticolis spasmodiques: Spasmes, tics, rhythmes du cou, torticolis, Paris, Masson & Cie, 1907.

4. Patterson, R. M., and Little, S. C.: Spasmodic Torticollis, J. Nerv. & Ment. Dis. **98**:571, 1943.

CHRONIC RHEUMATIC ENCEPHALITIS, TORSION DYSTONIA AND HALLERVORDEN-SPATZ DISEASE

CLEMENS E. BENDA, M.D.
WAVERLEY, MASS.

IT IS GENERALLY accepted that Sydenham's chorea, or chorea minor, is a manifestation of rheumatic fever. It was only logical, therefore, that McCulloch [1] (1938) should use the term "encephalitis rheumatica" for Sydenham's chorea, as had been done before him by Poynton and Paine [2] and by Greenfield.[3] Greenfield studied the pathologic features of chorea minor in patients who died during the acute stage of the illness. He observed round cell infiltration, consisting of lymphocytes and plasma cells, within the perivascular spaces. More impressive, however, than the infiltration of elements of the blood was the glial reaction of the brain tissue around the perivascular spaces. Sometimes there was present only this spotty glial reaction, which resembles that seen in poliomyelitis and von Economo's (lethargic) encephalitis. There was a great increase in vascularity, with congestion of the capillaries and even subpial hemorrhages. Greenfield expressed the belief that the picture resembled the acute stage of encephalitis lethargica. In less severe cases the involvement of the brain is not so damaging, and McCulloch pointed out that acute rheumatic encephalitis is one of the exudative manifestations of rheumatic fever, rather than a proliferative one. In less severe cases no structural change of the type of rheumatic nodules or scars were observed in the brain. This is probably the reason that chorea is commonly not followed by permanent paralysis, weakness or other neurologic alteration. McCulloch suggested, therefore, that the encephalitis of rheumatic fever is similar in its anatomic process to the arthritis, the acute pericarditis and the myocardial changes of an acute attack of rheumatic fever. The first changes

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This paper was read in part at the meeting of the Boston Society of Psychiatry and Neurology on Oct. 17, 1946.

From the Research Department of the Walter E. Fernald State School, Waverley, Mass.; the Wallace Research Laboratory at the Wrentham State School, and the Department of Neuropathology, Harvard Medical School.

1. McCulloch, H.: Encephalitis Rheumatica: Chorea Minor of Sydenham, J. Pediat. **13**:741, 1938.

2. Poynton, F. J., and Paine, A.: Researches on Rheumatism, London, J. & A. Churchill, 1913.

3. Greenfield, J. G.: The Pathology of Sydenham's Chorea, Lancet **2**:603, 1922.

in structures such as the joints, cartilage or heart are exudative. The acute phase, however, is frequently followed by other attacks, and the exudative manifestations may be replaced by proliferative lesions of the vessels, heart, joints and other organs.

In children, acute rheumatic encephalitis frequently precedes other manifestations of rheumatic fever; rheumatic heart disease, in particular, may not become manifest for months or years. The diagnosis of chorea therefore, by no means depends on the presence of an associated endocarditis. On the other hand, acute rheumatic fever is only rarely associated with cerebral implications, and patients who die during an acute attack of rheumatic fever commonly do not reveal any lesions in the brain. Theoretically, one would expect rheumatic fever to produce chronic proliferative encephalitis under certain conditions, but there is an obvious gap in present knowledge concerning the fate of patients who had had an attack of chorea minor. Scattered clinical observations suggest that some children do not go through an attack of chorea without permanent damage and lasting mental symptoms; even epileptic seizures may be observed. However, little systematic research has been done along this line, and the neuropathology of chronic rheumatic encephalitis remains practically unknown. The pertinent question, therefore, is this: Does chronic proliferative rheumatic encephalitis, similar to chronic rheumatic heart or joint disease, exist? If so, what are its specific manifestations?

In three successive publications, Winkelman and Eckel [4] discussed the pathologic changes in the brain associated with severe infections, toxemias and bacterial endocarditis. They observed productive endarteritis of the small cortical vessels, edema and fibrosis of the leptomeninges, areas of devastation (*Verödungsherde*) in the gray matter, small granulomatous proliferations and extensive changes in the nerve cells. Their cases included instances of bacterial infections, chronic tuberculosis, rheumatic fever and toxemias. The authors concluded that a great variety of infections and toxic agents are capable of producing a proliferative reaction of the smaller vessels and chronic encephalitis, for which Winkelman proposed the term "encephalosis," in analogy with the terms nephritis and nephrosis. Winkelman and Eckel expressed the opinion that their productive endarteritis was identical with the Nissl-Alzheimer endarteritis described in association with syphilis. In 1932 Winkelman and Eckel [5] added a publication on changes in the

4. Winkelman, N. W., and Eckel, J. L.: Productive Endarteritis of the Small Cortical Vessels in Severe Toxaemias, Brain **50**:608, 1927; Endarteritis of the Small Cortical Vessels in Severe Infections and Toxemias, Arch. Neurol. & Psychiat. **21**:863 (April) 1929; The Brain in Bacterial Endocarditis, ibid. **23**:1161 (June) 1930.

5. Winkelman, N. W., and Eckel, J. L.: The Brain in Acute Rheumatic Fever, Arch. Neurol. & Psychiat. **28**:844 (Oct.) 1932.

brain in acute rheumatic fever; in this paper they discussed the literature in detail and described the pathologic picture of this condition. The alterations consisted in proliferative changes in the small vessels and capillaries; "swelling" of the endothelial lining; numerous areas of devastation in the gray matter; meningeal infiltrations and meningeal fibrosis; formation of small nodules, composed of glia and mesodermal elements, and widespread cellular changes in the nerve cells. The observations of Winkelman and Eckel proved that acute rheumatic fever is a general infection and that the brain is frequently as severely involved as other organs, such as the heart and joints. Although studies show that the majority of alterations are exudative and may be reversible, it is obvious that a number of changes, such as the meningeal fibrosis and *Verödungsherde* and the granulomas, seen in some cases, are no longer reversible. These observations indicate that there may be a gradual transition to irreversible, chronic lesions, which may appropriately be termed productive encephalitis (Hassin [6]).

Von Sántha,[7] in 1932, described vascular changes in the central nervous system associated with rheumatic chorea. His observations were based on a case in which death occurred during an attack of chorea minor of four weeks' duration. There were proliferation of the intima and adventitia of the small vessels and similar changes in the capillaries, resulting in thick tubular bundles and "convolute formations." A fibrinous exudate, rich in iron, infiltrated the subendothelial layers. There were many areas of cortical devastation, and many of the smaller arteries were occluded with organized masses, which von Sántha interpreted as thrombi, but which were proliferative vascular changes, as I shall show later. He expressed the belief that the lesions of the cerebral vessels were similar to those in the vascular system of patients with rheumatic fever, and he concluded that these changes have a certain amount of specificity. This point was stressed by Bruetsch,[8] who since 1938 has published a series of papers on the pathology of the brain in chronic rheumatic fever. He demonstrated a proliferative endarteritis which resulted in complete occlusion of the smaller vessels, similar to that seen in vessels of the heart. He also established that these occlusions

6. Hassin, G. B.: Toxic Productive Encephalitis, J. Neuropath. & Exper. Neurol. **4**:354, 1945.

7. von Sántha, K.: Ueber Gefässveränderungen im Zentralnervensystem bei Chorea rheumatica, Virchows Arch. f. path. Anat. **287**:405, 1932.

8. Bruetsch, W.: Chronische rheumatische Gehirnerkrankung als Ursache von Geisteskrankheiten: Eine klinisch-anatomische Studie, Ztschr. f. d. ges. Neurol. u. Psychiat. **166**:4, 1939; Chronic Rheumatic Brain Disease as a Possible Factor in the Causation of Some Cases of Dementia Praecox, Am. J. Psychiat. **97**:276, 1940; The Histopathology of the Psychoses with Subacute Bacterial and Chronic Verrucose Rheumatic Endocarditis, ibid. **95**:335, 1938.

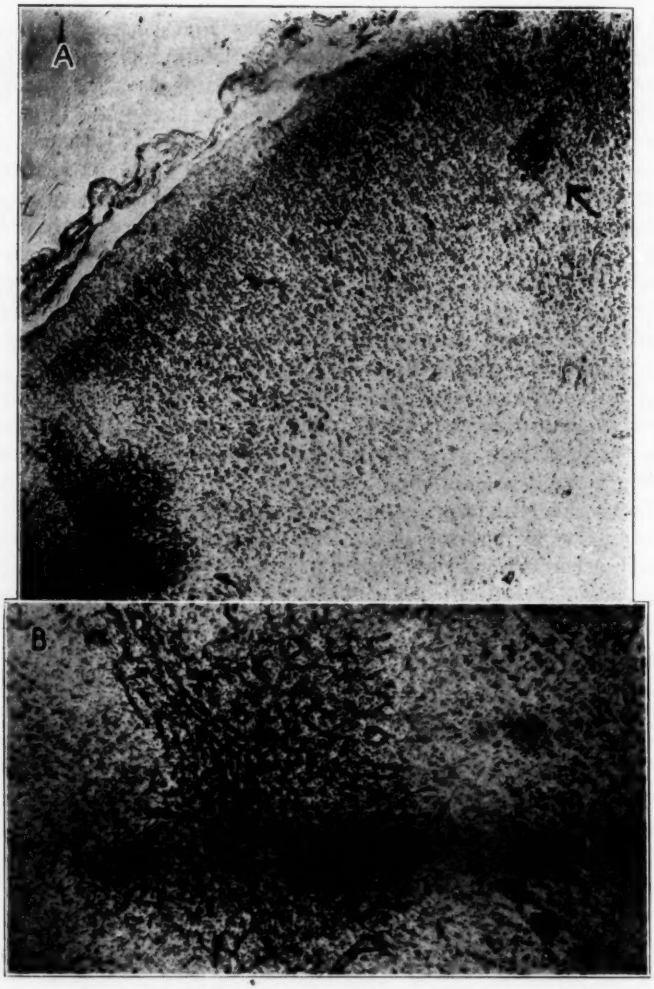

Fig. 1 (case 1).—*A*, cortical area, frontal lobe, showing several large and small areas of devastation (*Verödungsherde*). Two are filled with a dense pile of capillaries, surrounded by a pronounced microglial and oligodendroglial reaction. Other areas are devoid of cells. The arachnoid shows patchy prolifieration of fibrous tissue.

B, higher magnification of one of the scars with capillary proliferation. Note the destruction of nerve cells and the increase in glia, which is mainly of microglial and oligodendroglial type. There is no astrocytosis. Several of the smaller vessels in the vicinity of the scar are obliterated or partly occluded.

are due not to thrombosis but to proliferative changes of what he called endothelial cells. He observed numerous areas of devastation in the cortex, capillary proliferations and formation of peculiar granulomatous nodules, which consisted of glia and proliferated vascular tissue. He showed, therefore, that McCulloch's belief, i. e., that chronic proliferative changes do not occur after exudative encephalitis in rheumatic fever, is not correct and that acute rheumatic encephalitis may, indeed, become chronic productive meningoencephalitis, a point of considerable psychiatric importance. Despite a number of publications which deal with rheumatic encephalitis, and which are cited by the authors already mentioned, most general pathologists and neuropsychiatrists are not familiar with the pathologic and clinical implications of rheumatic encephalitis.

The following 4 cases are of interest because of the neuropathologic process, representative of chronic rheumatic encephalitis, and because of the neurologic manifestations in 2 cases of torsion dystonia (cases 3 and 4). In case 4, in addition to histologic alterations in the brain similar to those in the first 2 cases, hemosiderosis of the globus pallidus was so striking that the diagnosis of Hallervorden-Spatz disease was indicated. These observations throw a new light on the possible pathogenesis of this condition.

REPORT OF CASES

In the course of a study of the brains of 200 patients with various manifestations of mental deficiency, 2 cases were first observed in 1941 in which the pathologic changes differed essentially from those seen in any previous case.

CASE 1.—The patient had a poor family background; her mother was alcoholic and was thought to be syphilitic. The patient had been born by instruments. Her history stated that at the age of 3 years she had an acute attack of "brain fever" and convulsions. She was backward in walking and talking and speech was limited and not distinct. She was admitted to the Wrentham State School in 1915, at the age of 7 years. There she was untidy and difficult to manage. She would bite and scratch other children; at the same time, she was an affectionate child. Examination revealed an enlarged heart with a systolic murmur and mitral regurgitation. The Wassermann reaction of the blood was always negative. The intelligence quotient fluctuated considerably, from values as low as 35 to those as high as 43. She was slow and unable to do much, although no specific neurologic manifestations were observed. Her condition remained unchanged until the age of 31, when pulmonary tuberculosis developed in the apex of the righ lung, with smaller cavities and fibrosis. She died at the age of 35 years.

In the cortex of the brain were observed a number of areas which were lemon or butterfly shaped and which were either completely devoid of nerve cells and empty or filled with a bundle of proliferated capillaries and adventitial cells mixed with microglia. Many of the smaller capillaries and arteries were occluded. Some of the leptomeningeal vessels showed proliferation of mesothelial elements, at times with occlusion of the whole lumen. Small nodules were scattered along the leptomeninges (figs. 1 to 3).

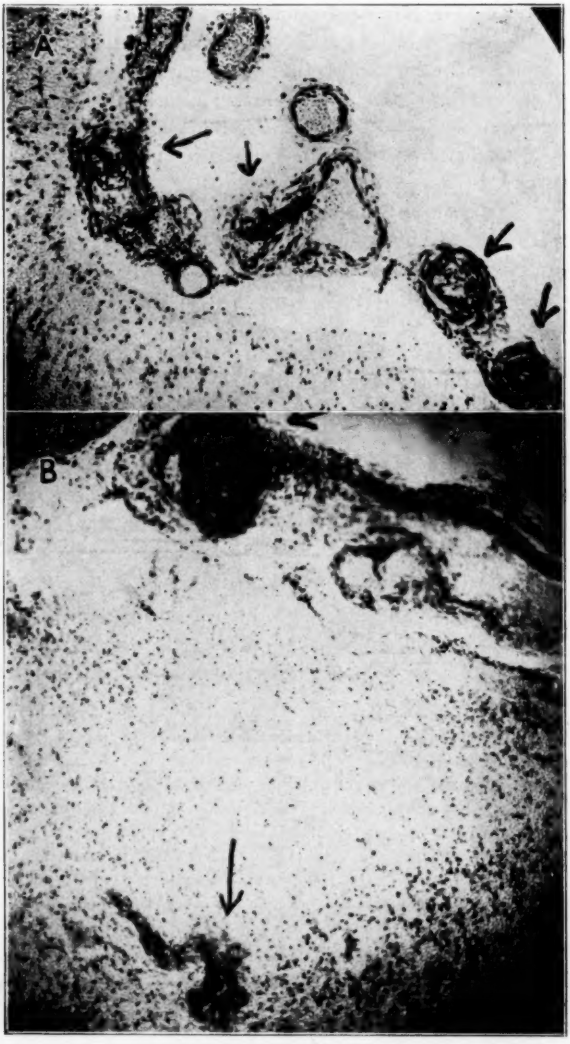

Fig. 2 (case 1).—*A*, group of meningeal vessels. Several of the arteries are completely or partially occluded by dense proliferation of fibrous tissue. The adventitial cells show irregular proliferation, but there is no true round cell infiltration of an acute inflammatory character.

B, meningeal vessel occluded by dense fibrous tissue, with partial canalization. The adventitial cells show irregular proliferation, and the arachnoidal lining is thickened. In the cortex are an acellular area and an occluded, tortuous cortical artery, with the walls thickened.

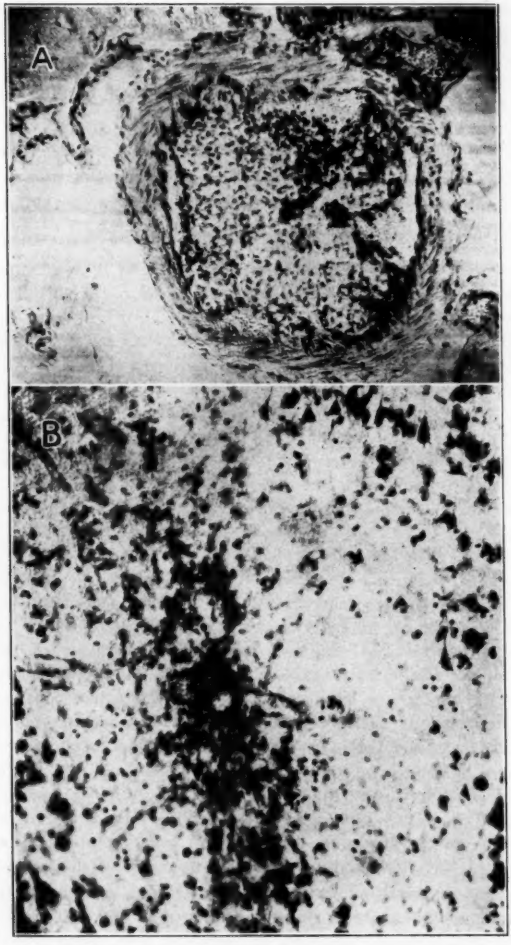

Fig. 3 (case 1).—*A,* meningeal artery under high magnification, showing proliferation of the subendothelial fibrous tissue in the lumen of the artery. The internal elastic coat is partially lifted or ruptured, and the endothelial cells form irregular groups within areas of proliferation of fibrous tissue.

B, cortical scar around a small vessel. Proliferating capillaries radiate in all directions. The wall of the larger vessel is thickened, and the surrounding area shows infiltration with fibrinous exudate. In the immediate neighborhood of the vessels is microglial and oligodendroglial proliferation. The nerve cells are destroyed.

Comment.—Clinically, the case did not present specific neurologic manifestations but was one of mental deficiency at an imbecile level, with a rather scattered correlation chart, indicating the possibility of cerebral lesions. A definite pathologic diagnosis could not be made, for the mother had had syphilis and there was therefore the possibility of congenital syphilis, in spite of the negative serologic reactions. The microscopic picture of the brain (figs. 1, 2 and 3) was confusing. At first, I believed that congenital syphilis was indeed present, but a more detailed examination and comparison with other cases of congenital syphilis led me to discount this diagnosis (Benda [9]). It was only after several more cases had been studied that the true nature of the lesions became evident. It may be added that the heart revealed definite evidence of mitral stenosis and rheumatic endocarditis.

Case 2.—A girl, born Oct. 28, 1919, began to walk at 12 months and to talk at 3 years of age. She was considered slow because she began to talk late, but she showed fair physical development. She had whooping cough, measles and scarlet fever. In April 1930, at the age of 10½ years, she had onset of chorea and was treated in the Beth Israel Hospital, Boston. A report from the hospital states that when the patient was first seen, in April 1930, approximaely one week prior to her admission, she complained of sudden onset of shaking, nervousness, pronounced twitching of the mouth and incoordinated movements of the arms and legs. These symptoms gradually became severer. There was no vomiting or fever. Physical examination revealed conspicuous movements of the arms and legs, twitching of the mouth and shaking of the head from side to side. The child improved somewhat for a few weeks, and then her condition became stationary. Examination of the heart revealed a faint systolic murmur. The patient was last seen in that hospital on Sept. 6, 1930, at which time there was general improvement, with little twitching. The diagnosis of chorea was made. However, she became more and more of a behavior problem and was admitted to the Wrentham State School at the age of 14 years and 10 months. At that time she was childish and played with dolls. With a chronologic age of 14 years 10 months, she had a mental age of 5 years 6 months and an intelligence quotient of 65. She was fairly well developed and nourished. At the age of 21, roentgenograms showed a tuberculous cavity in the apex of the left lung, and the patient died of tuberculous pneumonia two months later, in January 1941.

Autopsy revealed a fibrotic tuberculous process in both lungs. There was, however, no spread of the disease to other organs of the body. Vegetations on the cusps of the mitral valve were adherent and could not be stripped off. The diagnosis was old rheumatic endocarditis. Examination of the brain revealed no evidence of tuberculosis but showed endarteritis of the leptomeningeal vessels of the same type as that described in case 1 (fig. 5 *A*). Cortical scars, with areas devoid of nerve cells and some capillary proliferation, were noted (fig. 6 *B*). There were also demyelination and occlusion of vessels in the basal ganglia.

Comment.—In this case there was a definite history of chorea, of about six months' duration. After that time the involuntary movements and twitching ceased, but the child became a behavior problem and was

9. Benda, C. E.: Syphilis in Serum Negative Feebleminded Children, Am. J. Psychiat. **96**:1295, 1940.

obviously mentally deficient, so that she had to be admitted to a school for feebleminded children. She died of pulmonary tuberculosis.

The heart showed old rheumatic lesions. Evidence of meningoencephalitis consisted in occlusion of the smaller vessel; contorted, spiral-like capillaries with pronounced proliferation of adventitial histiocytes; areas of devastation; granulomatous nodules, consisting of mesodermal tissue and glia, and general changes in the nerve cells. The histopathologic picture was again different from that seen in cases of congenital syphilis or other infections and resembled closely that seen in the first case. Moreover, the lesions of the meningeal vessels were identical with those observed in the heart, kidneys and adrenal glands, indicating a common pathogenesis of all vascular lesions.

While motor manifestations of a chronic nature were not present in the first 2 cases, the next 2 cases presented a dramatic neurologic course.

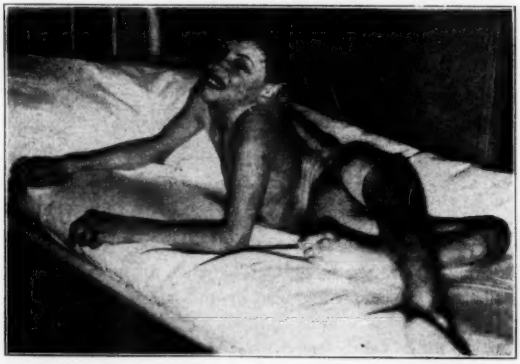

Fig. 4 (case 3).—Torsion spasm of the trunk, dystonia and spasticity of the legs in a patient aged 15 years.

Case 3.—The child was born in 1921, the fourth of a family of 6 siblings. One brother died at the age of 4 months of what was said to be "congenital heart disease." The other children were said to be normal. Birth was at full term without difficulty, and the early development was normal. The child began to talk at 8 months of age and was said to have walked at 14 months of age. At the age of 19 months she had what was called "brain fever." After this episode she was unable to walk and was severely deformed by a curvature of the spine. She did not talk for three years after this illness. She had occasional convulsions until the summer of 1931, when she was 10 years of age. These convulsions lasted sometimes for two and one-half hours. At the age of 11½ years she was admitted to the Wrentham State School. At that time she was poorly nourished and underdeveloped and was not able to sit or to walk. In 1937, when she was about 15 years of age, I made a neurologic examination.

The child was bedridden and unable to sit up or to stand, owing to extreme torsion of the trunk, which made her face turn toward her back (fig. 4). The trunk was bent to the left in a bow, and the head was drawn to the left shoulder.

The patient was able to move her head slightly toward the right, but the motion was performed with difficulty against spasms on the left. Both arms were used in coarse motions, with striking lack of coordination. The motions were jerky, and a great deal of choreoathetosis was present. If the patient became apprehensive and excited, the involuntary movements increased; if she relaxed, they ceased for a short time. The torsion spasms of the back likewise increased under stress and emotional upsets and disappeared at times. Both legs were stretched and crossed, and the patient was not able to overcome the severe spasticity. Both feet were in equinovarus position. When she was reclining, it was possible to separate the legs and to bend the left leg at the knee and at the hip joint. It was impossible to overcome the extension of the right leg. The knee jerk was very active on both sides, and application of any stimulus along the leg and foot increased the spasms. A Babinski sign was elicited in both feet. While the choreoathetoid movements spread over the head, neck and upper part of the trunk and the extremities, the legs remained spastic. Although she was unable to stand or to take any steps, even when supported, the child moved rapidly, and rather skilfully, along the floor by pulling herself with her hands. She was mentally alert and understood commands, but her speech was difficult to understand. In an attempt to talk, the face was contorted, and the mouth, tongue and neck showed violent choreoathetoid motions. There was also difficulty in swallowing. It was felt that the previous diagnosis of spastic cerebral paralysis, infantile type, was not correct and that the child had the condition described by Mendel [10] as torsion dystonia, or dystonia musculorum deformans (Oppenheim [11]).

The patient died at the age of 19½ years, of bronchopneumonia. During the last five years of her life she had failed somewhat in alertness and energy, but as a whole the progress of the neurologic condition was slow.

Autopsy.—The heart revealed mitral stenosis with a rigid ring, which admitted 1 finger only. The cusps were thickened, and the lower surface was covered with vegetations, which were adherent and could not be stripped off. One of the cusps was attached to the wall of the ventricle. The papillary muscles and the tendinous strings were thickened or bound together by masses of fibrous tissue. The tricuspid valve was also narrowed and admitted 1 finger only. The diagnosis was old rheumatic endocarditis with adhesions, vegetations and mitral stenosis. Examination of the brain revealed widespread lesions, with many indications of a still active encephalitis. The type of encephalitis could not be determined until a comparison of this case with the 2 cases previously described revealed similar lemon-shaped or butterfly-shaped acellular scars in the cortex, patchy nodular thickenings of the arachnoid, endarteritis of the small and medium-sized arteries in the meninges, some vascular occlusion and areas of demyelination, as well as of devastation. A new feature was represented by heavy deposits of iron in the globus pallidus and severe involvement of the basal ganglia, the brain stem and the cerebellum. While the pathologic process in the vessels and meninges seemed similar to that in the 2 previous cases, the localization was quite different in that in this case the basal ganglia and the cerebellum were most extensively affected.

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10. Mendel, K.: Torsiondystonie: Dystonia musculorum deformans, Monatschr. f. Psychiat. u. Neurol. **46**:309, 1919.

11. Oppenheim, H.: Ueber eine eigenartige Krampfkrankheit des kindlichen und jugendlichen Alters: Dysbasia lordotica progressiva, Dystonia musculorum deformans, Neurol. Centralbl. **30**:1090, 1911.

Comment.—The lesions in the heart, the history of crippling joint disease in infancy and the similarity of the pathologic processes in the brain to those in the previous cases are sufficient evidence that this case also was one of chronic rheumatic encephalitis.

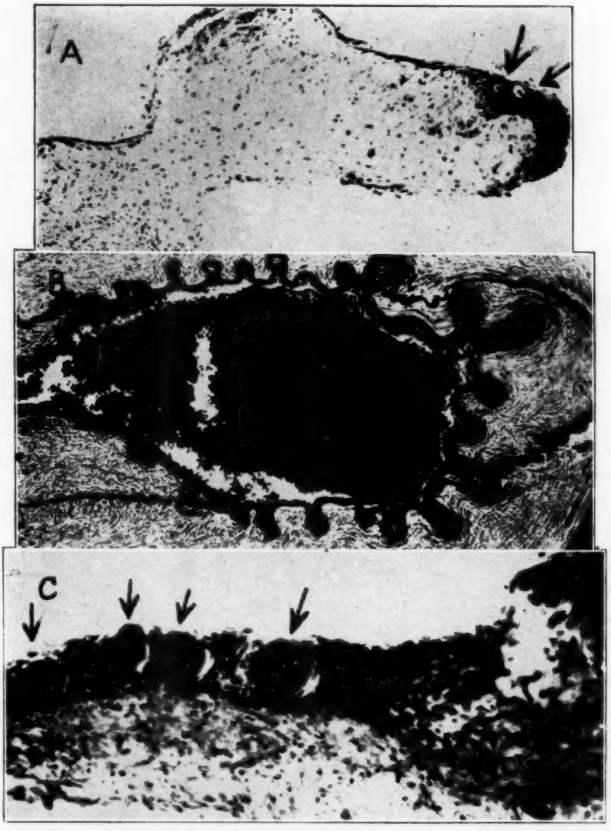

Fig. 5.—*A* (case 2), leptomeninges with irregular proliferation of the arachnoidal lining. At the tip of the meningeal loop is a group of small vessels which are partially or totally occluded. The leptomeningeal meshwork shows irregular proliferation.

B (case 4, an 11½ year old girl), basal artery, showing the healed stage of a vascular disease. Note the splitting of the internal elastic coat, with tremendous proliferation of fibrous tissue between the two sheaths. The vascular pathologic picture at this stage is nonspecific. It is significant, however, that encephalitis was associated with so much pathologic change in the vessels. See figure 7 *B* for a myocardial vessel in the same case.

C (case 4), higher magnification of the leptomeninges with arachnoidal lining. Note the similarity of the pathologic picture to that shown in *A*: complete occlusion of several vessels, irregular proliferation of the lining and thickening of the meningeal meshwork.

The existence of heavy deposits of iron or "pseudocalcium" in the globus pallidus led to reexamination of the brain in a fourth case, in which autopsy showed conspicuous deposits of iron. The case presented a problem from the clinical, as well as from the pathologic, point of view.

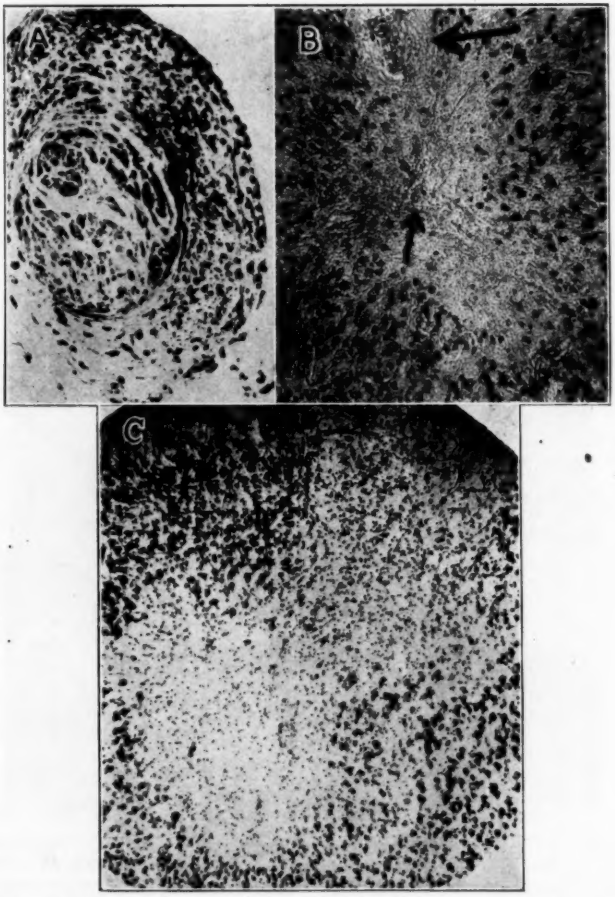

Fig. 6.—*A* (case 3), myocardial artery completely occluded by fibrous tissue, destruction of the internal elastic coat, irregular endothelial nests within proliferation of fibrous tissue and of adventitial histiocytes.

B (case 2), acellular scar within cortical layers, with completely occluded vessels within the scar.

C (case 3), acellular scar in the gray matter, similar to that in *B*.

CASE 4.—The patient, born in 1934, was the second child, her sister being normal. The patient was somewhat late in learning to sit up and to walk, and her speech was always defective. She learned, however, to move around without difficulty,

and when she was admitted to the Wrentham State School, at the age of 5 years, her intelligence quotient was 60 in one test and 67 in another. She had internal strabismus, and it was observed that her gait was on a rather broad base. The reflexes were active, but not abnormal; she was placed in one of the nurseries. Only in the course of the next few years was it noted that she was becoming progressively unsteady on her feet and that she fell frequently. In 1943, at the age of 9 years, it was obvious that she had failed and that the right side was stiffer than

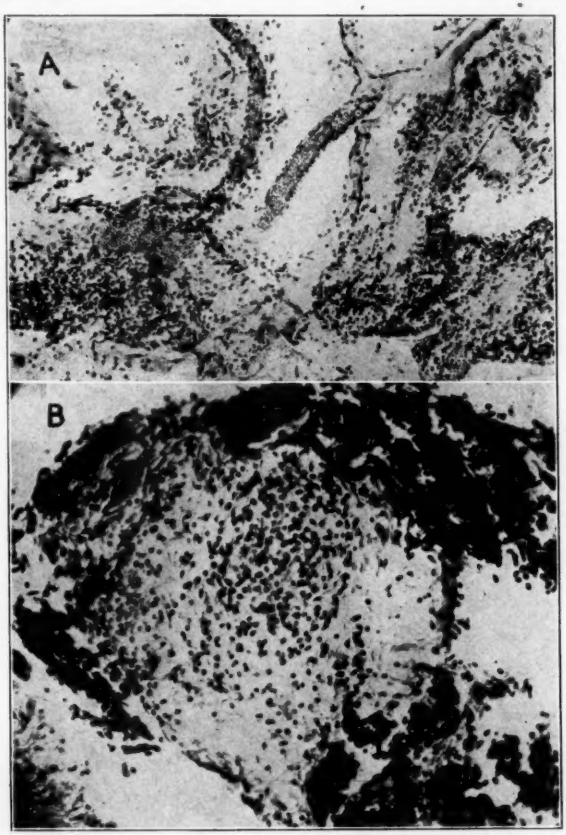

Fig. 7 (case 4).—*A*, section of leptomeninges over the cerebellum. Note the irregular thickening in the leptomeningeal meshwork with proliferation around the small vessels and moderate round cell infiltration.

B, myocardial vessel completely occluded by a process similar to that shown in figure 6 *A* (case 3). Only a small area of the original vessel wall is recognizable. The lumen of the vessel is completely occluded, and the adventitia is greatly thickened; smaller vessels are also occluded. There is some round cell infiltration.

the left. The reflexes were increased, and the right arm was held in flexion. The right leg was moderately spastic. The Babinski sign was present. The movements of the face were slow and grimacing. Later the left leg became involved. The

gait became spastic, and finally the legs became crossed. The face was ready to smile, but slowly and in a compulsive manner. In 1944 the child was so severely handicapped that she was transferred to this hospital. After that time, I saw the child almost daily and witnessed the progressive deterioration of her condition up to the very end, which occurred a year later, in 1945, at the age of 11½ years.

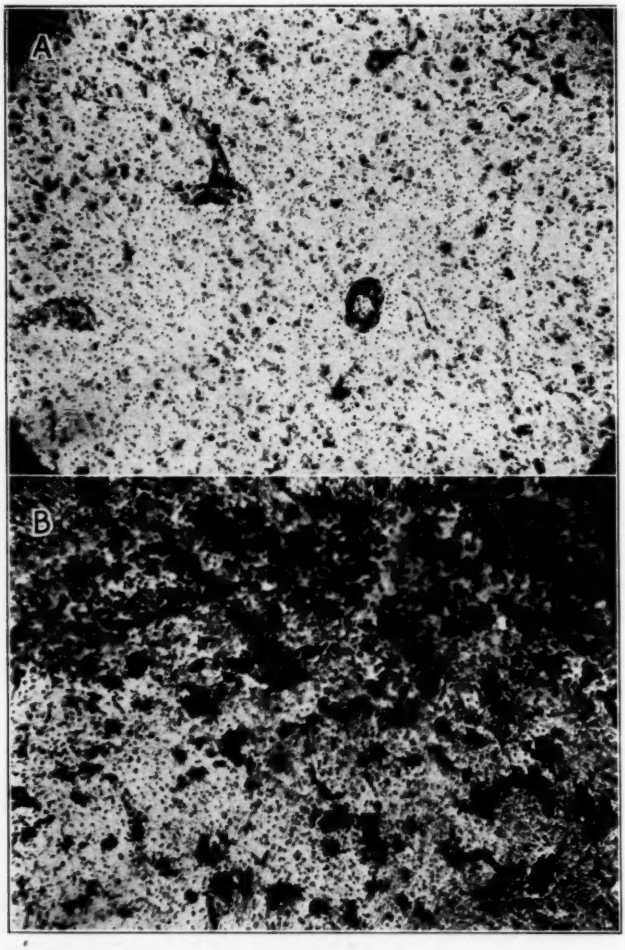

Fig. 8.—*A* (case 3), globus pallidus, with hemosiderosis, consisting of small, dustlike concrements in this area. The cross section of the artery shows a thickened ring of fibrinous exudate. The other vessel, cut lengthwise, shows a thickened wall. The nerve cells are destroyed. There is diffuse glial proliferation.

B (case 4), area of globus pallidus with tremendous amount of hemosiderosis, rather large concrements of iron, complete destruction of nerve cells and considerable gliosis.

Autopsy.—The liver appeared normal both on gross and on microscopic examination. It weighed only 550 Gm., instead of the 900 Gm., normal for the age of this patient. There was no conspicuous lesion of the heart, but the myocardium showed many small white, fibrotic strands and nodules. In the aortic arch there was a considerable number of raised, yellowish plaques, an unusual lesion in a child of 11 years. The pericardial sac contained an increased amount of yellow fluid.

The brain was soft and did not entirely fill the cranial cavity. It weighed 1,090 Gm. and was of good shape, with normal convolutional patterns. Coronal sections revealed that the globus pallidus on each side was conspicuous by its reddish brown color. This was so striking in the fresh specimen that it looked as though some one had colored the pallidum to demarcate it in an anatomic specimen. After a few weeks' fixation in dilute solution of formaldehyde U.S.P., the brownish color faded away. Microscopic sections of the globus pallidus revealed a huge amount of iron, as demonstrated by the Turnbull reaction. There was a considerable amount of glia, consisting mainly of astrocytes. The pathologic process, however, was by no means restricted to the globus pallidus or to the "extrapyramidal" system, but was widespread and affected the cortex of the cerebrum and cerebellum as much as the basal ganglia. There was extensive capillary fibrosis, with all the smaller vessels tortuous and prominent. The walls of the vessels were thickened. Many perivascular spaces were enlarged and filled with a fibrous meshwork. The tissue outside the perivascular spaces was thinned and showed demyelination or necrosis. The leptomeninges above the sulci were thickened. The arachnoidal lining showed patchy nodular thickening. Granulomatous nodules were also observed along the walls of the lateral ventricles and in the choroid plexuses. The ganglion cells were in a state of widespread chromatolysis and shrinkage, with pronounced oligodendroglial and microglial reaction. The cerebellum was most severely involved, with meningovascular lesions, degeneration of the Purkinje cells, degeneration of the granular layer and pronounced perivascular fibrosis, enlargement of the perivascular spaces with weblike nests and occlusion of some vessels. The histopathologic picture indicated chronic productive meningoencephalitis. Comparison with the other cases in this series suggested the same pathogenic factors. The histologic condition of the globus pallidus suggested the diagnosis of Hallervorden-Spatz disease.

Comment.—The clinical picture in this case was extremely puzzling. In a child who was somewhat slow, but who had learned to walk and talk, a progressive neurologic condition was observed, which started in the right leg. The patient began walking on her toes, and the leg became stiff. Involvement of the right arm followed and for a certain period a unilateral condition was present, suggesting a localized lesion in the left hemisphere. Soon, however, the left foot was involved, and finally the condition was bilateral. The gait was stiff and unsteady. Later, spasticity was so extreme that the legs were crossed and walking was impossible. The trunk became distorted; the spine was drawn to the side and forward, and the head was bent backward. At the peak of the illness the patient was bedridden. The mouth was open and the tongue protruded. There were constant athetoid movements of the tongue, face, neck, trunk and arms. Swallowing was difficult, and speech became unintelligible. The patient was responsive and understood well. She smiled frequently and readily, but the response came slowly and seemed

compulsory. She usually lay on her side, bent in a semicircle. A Babinski sign was elicited on both sides. The most likely diagnosis seemed to be hepatolenticular degeneration (Wilson's disease), but hepatic tests failed to show any abnormalities and the abdomen always appeared normal on palpation. Friedreich's disease (hereditary sclerosis, spinal form) was considered, the cerebellar system being chiefly involved. It was also felt that the possibility of chronic encephalitis must be considered seriously.

Study of the autopsy material excluded the diagnosis of hepatolenticular degeneration, for the liver was normal. The striking accumulation of iron in the tissues of the globus pallidus suggested the diagnosis of Hallervorden-Spatz disease. A study of the meningovascular system, the cortex and the cerebellum, however, revealed so many lesions that it appeared incorrect to consider the process a mere degenerative disease of the basal ganglia. There was ample evidence of chronic productive encephalitis which was still in a progressive state and which involved the cortical gray matter as well as the white matter and the basal ganglia. Comparison with the lesions in the other cases indicated the diagnosis of chronic rheumatic encephalitis.

COMMENT

The 4 cases presented here are of interest from a neurologic, as well as a clinical, point of view. There can be little argument that all cases presented a characteristic picture of chronic productive encephalitis, as described by Winkelman and Ekel,[12] Hassin,[6] Bruetsch [8] and others. Winkelman and Eckel stated the opinion that the encephalitis of rheumatic infection is nonspecific. They expressed the belief that many types of chronic infection and toxemia, including tuberculosis, produce the chronic meningovascular changes and productive encephalitis of the same type and that the vascular lesion is identical with the Nissl-Alzheimer endarteritis which has been described in cases of syphilitic conditions. Von Sántha [7] and Bruetsch [8] stated that the picture of rheumatic encephalitis is, on the contrary, similar to that of syphilis. I agree that there is a similarity of chronic infectious lesions to syphilitic alterations. My material included 5 cases of congenital syphilis, 2 of which have previously been reported.[9] In a histologic study of meningoencephalitis syphilitica and Nissl-Alzheimer endarteritis, I observed that the histologic features of meningovascular syphilis are so typical that the diagnosis can be made even in the presence of negative serologic reactions. Although minor items, such as those which are characteristic of any productive encephalitis, are similar in many conditions, Nissl-Alzheimer endarteritis consists in proliferation

12. Winkelman and Eckel, footnotes 4 and 5.

of the endothelial cells, which narrows the lumen of the vessel, while the adventitial cells also proliferate and form dense cellular granulations. The meningeal fibrosis is diffuse. Moreover, even in the chronic type of Nissl-Alzheimer endarteritis there are always vessels with cuffing and evidence of infiltration with lymphocytes and plasma cells. Although in my first case the history suggested a diagnosis of congenital syphilis, a histopathologic study revealed such striking differences between the picture of congenital syphilis and the encephalitis present in this case that congenital syphilis could be excluded.

There remains, however, the question how the histopathologic diagnosis of rheumatic encephalitis can be established. While it is true that many bacterial and toxic agents may cause productive changes in the brain and result in proliferative vascular reactions, the histopathologic picture of chronic rheumatic encephalitis goes far beyond what has been seen in other conditions. As has been pointed out, in this condition one is dealing with a meningoencephalitis in which the vascular system undergoes alterations that are quite different from any endothelial "swelling" or proliferation. Only Bruetsch has given an accurate description of these changes. The vessels are occluded by proliferations of fibrous tissue, which were described by von Sántha as thrombotic and by Bruetsch as endothelial proliferation. It is to be noted, however, that the proliferation is produced not by the endothelial cells but by the subendothelial fibrous tissue, which either breaks through the internal elastic membrane or penetrates through primary damage of that lining. These fibrotic nodules contain a few endothelial nests but are composed mainly of fibrous tissue. Characteristic also is the amount of fibrinous exudate into the subendothelial tissue, which gives a dark blue staining reaction and which frequently contains iron, as was also observed by von Sántha. This fibrinous exudation can be seen likewise around the capillary proliferations. The leptomeninges are fibrotic, but at the same time irregular in their proliferation, and the arachnoidal lining often forms nodules, in which small occluded vessels may be seen. The cortical gray matter is conspicuous by virtue of the tortuous capillaries and small vessels and the patchy acellular areas. It may be mentioned that, although small perivascular areas of loss of cells are not rare in other conditions, these areas of devastation are rather characteristic and were not found in any of the control cases. Since more than 50 per cent of the patients forming my control material died of tuberculosis, frequently in an advanced stage, it can be stated that tuberculosis does not produce changes similar to those of rheumatic encephalitis. The changes in the nerve cells are, of course, nonspecific, and the perivascular necrosis and enlargement of the perivascular spaces are associated with cerebral edema and many other types of encephalitis.

While the chronic stages of rheumatic encephalitis lead to a characteristic meningoencephalitis, the diagnosis of the rheumatic nature of such an encephalitis rests on the evidence that the vascular changes in the brain are of the same nature as those in the heart, blood vessels and other organs. In 3 of my cases the condition of the heart indicated an old rheumatic endocarditis and myocarditis, and in the fourth case some myocardial scars suggested at least a similar pathogenesis. If the identity of the vascular changes in various organs, including the brain, can be demonstrated, the evidence that the pathologic process is of rheumatic origin rests on those histopathologic features which the general pathologist considers significant for rheumatic infection. This situation has been well discussed in various publications dealing with the diagnosis of vascular lesions in rheumatic fever.

As von Glahn and Pappenheimer [13] pointed out:

> . . . In the present uncertainty as to the causative agent of rheumatic fever, it is not possible to establish with finality the rheumatic nature of any given lesion. However, the frequent or constant association of a lesion with the clinical or pathologic features of rheumatic fever and its resemblance to other lesions generally recognized as associated with rheumatic infection, are presumptive evidence in favor of its rheumatic origin. Additional support is gained if the lesion in question has histologic features which are distinctive and which are not encountered in other known diseases. The specificity of the Ashoff nodule, indeed of all rheumatic cardiac lesions, rests upon no firmer foundation than this.

MacCallum,[14] who discussed rheumatic vascular disease extensively in his textbook, concluded that "all this is described at such length to indicate its unique character which marks out rheumatism as a disease quite different from any other we know."

HEMOSIDEROSIS OF THE GLOBUS PALLIDUS

It was noted that in cases 3 and 4 a considerable deposit of iron was observed in the globus pallidus. The character of those concrements could be determined by the Turnbull reaction, which demonstrated that the concrements were iron, and not calcium, by the dark bluish or black color. The globus pallidus was filled with concrements of material which had mulberry form or a fine, dustlike appearance. In Nissl preparations the color varied from dark blue to green and brown. The material was both extracellular and intracellular, and in silver stains many spots resembled plaques of the Alzheimer type, as seen in cases of senile disease. Plaques, however, were not observed in the cortex. Strass-

13. von Glahn, W. C., and Pappenheimer, A. M.: Specific Lesions of Peripheral Blood Vessels in Rheumatism, Am. J. Path. **2**:235, 1926.

14. MacCallum, W. G.: A Text-Book of Pathology, Philadelphia, W. B. Saunders Company, 1936.

mann [15] made an extensive study of the occurrence and importance of hemosiderin. He observed formation of hemosiderin after traumatic hemorrhages and in cases of spontaneous hemorrhage and of thrombosis. In a third group, he noted hemosiderin-like substances in selected areas of the brain without preceding hemorrhage. The 2 youngest patients in that group were 16 years of age, but, as a whole, Strassmann found that there is some relation between the amount of iron and the age and that the hemosiderin content increases with age. In the globus pallidus he frequently noted incrustations of blood vessels with iron salts and free iron without hemorrhage, and he concluded that the increased iron content is "a manifestation of an involutional process irrespective of the age of the patient or the duration and type of the illness." It is well known that increased iron content is frequent in various types of encephalitis and is by no means specific. In my third case the increase of iron in the globus pallidus was still within that to be expected in a case of chronic encephalitis, and the diagnosis of Hallervorden's disease was not made. In the fourth case, however, the iron in the globus pallidus was so conspicuous as to justify the diagnosis of Hallervorden-Spatz disease.[16] It seems pertinent, therefore, to reexamine the question whether Hallervorden-Spatz disease is a pathologic entity and a "degenerative" disease, as all earlier writers have claimed. It may be mentioned that in 1922 Hallervorden and Spatz described a family of 5 members in which, after an apparently normal development, at an age between 8 and 10 years extrapyramidal hyperkineses made their appearance, with a resulting picture resembling Wilson's disease and death in the thirties. Instead of the changes common in Wilson's disease, a huge amount of iron pigment, with degeneration of the globus pallidus and substantia nigra, was seen. In 1927, Kalinowsky [17] described another case of the familial incidence of the same progressive "extrapyramidal" disease in 2 brothers.

Analysis of these cases reveals that the claim of an "extrapyramidal" disease does not hold by present criteria. In Kalinowsky's first case

15. Strassmann, G.: Hemosiderin and Tissue Iron in the Brain: Its Relationship, Occurrence and Importance, J. Neuropath. & Exper. Neurol. **4**:393, 1945.

16. Hallervorden, J., and Spatz, H.: Eigenartige Erkrankung im extrapyramidalen System mit besonderer Beteiligung des Globus pallidus und der Substantia nigra, Zentralbl. f. d. ges. Neurol. u. Psychiat. **79**:254, 1922. Hallervorden, J.: Ueber eine familiäre Erkrankung im extrapyramidalen System, Deutsche Ztschr. f. Nervenh. **81**:204, 1924.

17. Kalinowsky, L.: Familiäre Erkrankung mit besonderer Beteiligung der Stammganglien, Monatschr. f. Psychiat. u. Neurol. **66**:168, 1927; Die Hallervordensche Krankheit, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol 16, p. 874.

the child developed normally up to the age of 3 years, when he became somewhat awkward in physical exercises. At the age of 10 years the gait was conspicuously abnormal. The legs became stiff. At the same time vision was found to be impaired. At the age of 12 years the arms became involved, being stiff and the motions awkward. Finally there was an equinovarus position of both feet. The reflexes were increased. There were knee clonus and a bilateral Babinski sign. Movements of the arms were described as ataxic, and some tremor was noted. The same progressive symptoms developed in a younger brother. There were continuous slow, involuntary movements of the head, with constant compulsive laughing. The tongue was in permanent motion of an athetoid character. Speech was slow, explosive and monotonous. Both arms were affected with slow, athetoid movements. There was mental deterioration. The older brother died at the age of 31 years.

The main pathologic change was the brownish discoloration of the globus pallidus and the substantia nigra, due to huge deposits of iron in these nuclei. There was considerable gliosis. In addition, many lesions were present in the cortex and the cerebellum. The leptomeninges were thickened, with a few round cells within the fibrous meshwork. Some of the vessels showed a moderate increase in the walls but no infiltration. The anatomic descriptions of Hallervorden and of Kalinowsky indicate that the attention of these authors was centered on the basal ganglia, the pathology of which was just entering a decade of great vogue. While they did not pay much attention to other parts of the brain or to the vascular system, it is to be noted that the development of the illness in their cases was identical with that described in case 4 of my series. My patient died at the age of 11 years, at the peak of the course of an active, progressive inflammatory disease, while Hallervorden's and Kalinowsky's patients lived into the thirties. It is possible, therefore, that at the older age the acute encephalitis had been arrested and regressive changes and degenerative processes dominated the picture. It is noteworthy that, in contrast to von Economo's (lethargic) encephalitis and postencephalitic parkinsonism, this disease involves the pyramidal system as much as the extrapyramidal. Especially in the early stages pyramidal symptoms dominate the picture.

The clinical observations and the pathologic picture in the cases of so-called Hallervorden-Spatz disease indicate that (1) the presence of heavy deposits of iron does not justify the establishment of a morbid entity, (2) that the disease is not one of the extrapyramidal system alone, (3) that there is not sufficient evidence for classification of the process as "degenerative" and (4) that at least some of the cases are identical with those that have been described from a clinical aspect as torsion dystonia or torsion spasms.

TORSION DYSTONIA

Dystonia musculorum deformans, torsion spasms or torison dystonia has been observed usually to develop in children at about the age of 9 years and become most conspicuous in adolescents of teen age. In 1919, Mendel [10] collected 20 cases from the literature and added 2 cases of his own, which he published in a monograph. Taylor,[18] in 1920 pointed out that Mendel had missed the cases published in the American literature, especially the 6 cases reported in detail by Hunt,[19] in 1916. Taylor criticized Mendel's attempt to establish a new morbid entity, emphasizing that the clinical manifestations vary to a great extent and that this disease is apparently only a variation of lenticular degeneration. This point of view was well taken with respect to the fact that no new autopsy reports were available and that several cases of torsion dystonia were later proved at autopsy to be cases of hepatolenticular degeneration.

Since many descriptions in textbooks and in journals are not entirely correct, and since there is considerable argument about the true character of this frequently misinterpreted disease, it is worth while to go back to the original descriptions collected by Mendel.

Schwalbe [20] was the first to describe 3 cases under the title "A Particular Form of Tonic Cramps with Hysterical Symptoms." The 3 patients were siblings. The oldest, a girl aged 17, began at the age of 11 to walk on the toes of her left foot. This symptom appeared temporarily at first but gradually the left foot assumed an equinovarus position. Later the right foot followed. The patient was then still able to walk, but only on her toes. Gradually, the trunk became bent forward, while the head was bent backward. There were uncontrolled movements back and forth, and the trunk appeared to be drawn back spasmodically. The left hand was drawn to the back, and sudden, jerky movements developed in both extremities. Physical examination at that time revealed an equinovarus position of both feet, atrophy of the legs and a Babinski sign on the left; presence of the knee and ankle jerks was doubtful. The patient presented a mixture of voluntary and involuntary movements of a type of chorea and tics. In a younger brother the same symptoms developed one year after those of his sister. In his case the symptoms began in the right foot. There were prominent choreoathetoid movements, in addition to the scoliosis and the distortion of the trunk. A third child fell ill a year later, and the illness again began in the right

18. Taylor, E. W.: Dystonia Lenticularis, Arch. Neurol. & Psychiat. **4**:417 (Oct.) 1920.

19. Hunt, J. R.: The Progressive Torsion Spasm of Childhood: Dystonia Musculorum Deformans, J. A. M. A. **67**:1430 (Nov. 18) 1916.

20. Schwalbe, W.: Eine eigentümliche tonische Krampfform mit hysterischen Symptomen, Inaug. Dissert., Berlin, G. Schade, 1908.

foot. Schwalbe discussed the differential diagnosis and concluded that his cases belonged in the category of *maladie des tics,* the condition probably being a heredodegeneration. Ziehen [21] observed 2 cases of this condition. The disease began in the right foot in a way similar to that in the other children. The body showed tonic and choreoathetoid movements, increasing under excitement. An extreme lordosis developed with dysarthria. Oppenheim [11] described the case of a girl aged 13 in whom the illness began at the age of 9 years with abnormal use of the right foot. Later the left foot was similarly affected. Gait became increasingly difficult because of the distortion of the trunk. There were extreme lordosis, grotesque movements of the body, hypotonia of the knee and ankle joints and weakness of knee and ankle reflexes. In another girl, aged 14, the illness started with cramps in the hand at the age of 7 years, when the patient learned to write; but later it was noticed that the right foot was held in abnormal position and that the patient walked on her toes. Abnormal use of the left foot followed a year later.

A perusal of the 20 cases collected by Mendel reveals a surprising monotony and only a few variations of the symptoms. A peculiar neurologic condition begins most frequently in the right foot and then involves the right arm and later the left side. The undoubtedly spastic symptoms of pyramidal involvement, consisting in the equinovarus position, the Babinski reflex and anomalies of the knee and ankle reflexes which are first increased and may later either become of doubtful presence or disappear, are accompanied with choreoathetoid movements of the trunk, face, tongue and arms. The disease usually develops in children before the age of 10 years, although most patients do not come under medical observation before they are in their teens. Headache is frequent. There are also cramps in the extremities, pain and spasm of the trunk. Unfortunately, no autopsy observations were available for Mendel's monograph. He concluded that the disease represented a morbid entity, which could be differentiated from *athetose double,* Huntington's chorea and Wilson's disease. Although several authors suggested the possibility of a hysterical condition, Oppenheim lent his authority in favor of an organic disease, and most authors have accepted this interpretation (Peritz [22]).

As already mentioned, no autopsy report was available for Mendel's monograph except in Thomalla's [23] case, which was apparently an instance of hepatolenticular degeneration (Wilson's disease), since there was cirrhosis of the liver. Taylor [18] mentioned that in Flatau and Ster-

21. Ziehen, T.: Ein Fall von tonischer Torsionsneurose, Zentralbl. f. d. ges. Neurol. u. Psychiat., 1911, p. 109.

22. Peritz, G.: Die Nervenkrankheiten des Kindesalters, Leipzig, 1932.

23. Thomalla, C.: Ein Fall von Torsionsspasmus mit Sectionsbefund und seine Beziehungen zur Athetosis double, Wilsonsche Krankheit und Pseudosklerose, Symptomen, Inaug. Dissert., Berlin, G. Schade, 1908.

ling's [24] case, cited by Mendel, autopsy later revealed cirrhosis of the liver. The same is true for the cases reported by Wimmer,[25] Hall [26] and Schneider.[27] As the titles of the publications by the last 2 authors indicate, these authors concluded that torsion dystonia is a symptom of Wilson's hepatolenticular degeneration. However, not all cases of torsion dystonia belong to this disease. Davison and Goodhart [28] concluded:

> It is questionable whether all the cases are the true degenerative type of dystonia musculorum deformans. Some apparently are post-encephalitic extrapyramidal disorders with dystonic fragments; some are variants of Wilson's disease or pseudosclerosis and others are strongly suggestive of chorea.

As will be seen, this is the only logical conclusion possible, and the present confusion is due not to the fact that all these symptoms are manifestations of the same pathologic process, but that clinical and biochemical means of differential diagnosis are still unsatisfactory. It is more than ever necessary to isolate these symptoms according to their pathogenesis because each entity postulates a different therapeutic approach.

Kroll [29] analyzed the "hyperkinetic" syndrone, including chorea, athetosis duplex and torsion spasm, and concluded that the spasm of torsion dystonia is a manifestation of athetosis which differs in its somatic localization from the peripheral type. He asserted that while in athetosis the distal ends of the extremities are mainly affected, torsion dystonia is an athetosis of the muscles of the trunk, through which the strange corkscrew motions of the body and the compulsive distortion of the trunk are produced. My own cases, as well as Kroll's and Ford's [30] observations, emphasize that in most cases of this disorder, the distal segments of the extremities are also involved and that the head, tongue and muscles of deglutition and speech are affected. Kroll's conclusion that the whole group represents a striatal syndrome, in contrast to the

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24. Flatau and Sterling: Progressiver Torsionsspasmus bei Kindern, Zentralbl. f. d. ges. Neurol. u. Psychiat. **7**:586, 1911.

25. Wimmer, A.: Études sur les syndromes extra-pyramideau: Spasme de torsion progressive infantile: syndrome de corps strié, Rev. neurol. **28**:952, 1921.

26. Hall, H. C.; La dégénérescence hépato-lenticulaire, Paris, Masson & Cie, 1921.

27. Schneider, E.: Torsionspasmus, ein Symptomkomplex der mit Leberzirrhose verbundenen progressiven Lenticulardegeneration, Zentralbl. f. d. ges. Neurol. u. Psychiat., 1920, p. 39.

28. Davison, C., and Goodhart, S. P.: Dystonia Musculorum Deformans: A Clinco-Pathologic Study, Arch. Neurol. & Psychiat. **29**:1108 (May) 1933.

29. Kroll, M.: Die neuropathologischen Syndrome, zugleich Differentialdiagnostik der Nervenkrankheiten, Berlin, Julius Springer, 1929.

30. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood, and Adolescence, Springfield, Ill., Charles C Thomas, Publisher, 1937.

pallidal syndrome, is not entirely supported by pathologic observations. As has previously been shown, the cerebellum, the cortex and the whole extrapyramidal system are so involved that an attempt to localize the symptoms is premature. Wechsler and Brock [31] stressed the frequent occurrence of a "myostatic" form of torsion dystonia and emphasized the rigidity which frequently enters the picture.

While torsion dystonia is mainly a clinical concept without reliable autopsy observations, the Hallervorden-Spatz disease is primarily a neuropathologic concept which was established as a specific disease of the basal ganglia, in contrast to the lesions of hepatolenticular degeneration (Wilson's disease).

In case 4 of my series the clinical pattern follows exactly that described by Mendel, Hunt, Ford, Wechsler and others and autopsy revealed the lesions of Hallervorden-Spatz disease. Comparison of other cases of the two types shows that in Hallervorden's cases the disease frequently developed as a torsion dystonia and the pathologic picture of torsion dystonia in several cases revealed deposits of iron or "pseudocalcium" in the tissues (Ford).

Since torsion dystonia was frequently observed in siblings, it has been assumed that it is a heredodegenerative disease. Moreover, since several cases have been observed in Jewish children, a racial predominance has been claimed. Neither argument stands critical examination. In many cases observed only one member of the family was affected, and in many cases no alleged racial selectivity could be demonstrated. The concept of a "degenerative" disease, which I [32] have criticized on several occasions, is of little value. If the disease is a hepatolenticular degeneration, it is a "metabolic," rather than a degenerative, disorder. If it is of infectious origin, the concept of a degenerative disease only blocks the way toward proper therapeutic measures at an appropriate time. Hallervorden's patients, as well as Kalinowsky's, lived beyond the age of 30 years, while patients 3 and 4 of my series died at the ages of 19 and 11 years, respectively. It is possible that in older patients the nature of the original disease is no longer discernible. In my patients, who died at the peak of the disease process, the true nature of the pathologic process was clearly revealed.

SUMMARY

1. In a certain, as yet unknown, percentage of cases, rheumatic infection is associated with rheumatic encephalitis. Although chorea

31. Wechsler, I. S., and Brock, S.: Dystonia Musculorum Deformans with Special Reference to a Myostatic Form and the Occurrence of Decerebrate Rigidity Phenomena: A Study of Six Cases, Arch. Neurol. & Psychiat. **8**:538 (Nov.) 1922.

32. Benda, C. E.: Neuropsychiatric Aspects of Mental Deficiency, North Carolina M. J. **8**:72 (Feb.) 1947.

minor is the best known manifestation of rheumatic encephalitis, infection of the brain may occur with other symptoms of less alarming nature or may remain asymptomatic for a time and lead insidiously to mental deterioration or to behavior problems.

While acute rheumatic encephalitis is apparently of an exudative and reversible nature, repeated attacks or chronic rheumatic encephalitis produces a characteristic productive meningoencephalitis.

In this paper the occurrence of chronic rheumatic encephalitis is demonstrated by a clinicopathologic report of 4 cases.

1. The first case was one of asymptomatic chronic rheumatic encephalitis, with mental deficiency as the main symptom. The clinical history was not relevant, and the diagnosis of chronic rheumatic encephalitis was made from the peculiar cerebral lesion, which indicated a morbid process distinguishable from congenital syphilis and chronic bacterial infection.

2. The second case was that of a child whose development was apparently normal up to the age of 10 years, although she had whooping cough, mumps and measles. Chorea minor developed, and she was treated in a hospital for six months. After that time the child appeared infantile and silly, with evidence of mental retardation. The patient died at the age of 21 years. The lesions were similar to those in case 1.

3. In case 3 the patient apparently developed normally up to the age of 19 months. At that time she had an acute infectious disease which was diagnosed as "brain fever." After that the patient was badly deformed, with curvature of the spine and inability to walk and talk. She had convulsions occasionally. At the age of 15, she revealed a rather characteristic picture of torsion dystonia, with choreoathetoid movements of the arms and hands, face and tongue; torsion spasm of the trunk and spastic paralysis of the legs with crossing; increased reflexes and a bilateral Babinski sign. The neurologic condition became progressively worse, but at an extremely slow rate. The patient died at the age of 19½ years. Histopathologic examination revealed evidence of chronic encephalitis with numerous characteristic features, similar to those seen in cases 1 and 2.

4. In case 4 development was fairly normal, although slow, up to the age of 4 years, when there was abnormal posture of the right foot, resulting in an equinovarus position and spasticity of the leg. The right arm was gradually held in flexion. Later the left side was involved. At the age of 9 years the child exhibited the picture of torsion dystonia. The legs were spastic and crossed, presenting a bilateral Babinski sign; the trunk showed mobile spasm and distortion, and the face, tongue, neck, arms and hands exhibited choreoathetoid movements. The child died at the age of 11. Histopathologic examination revealed extreme

hemosiderosis of the globus pallidus (Hallervorden-Spatz disease) and, in addition, evidence of a chronic productive meningoencephalitis, with involvement of the cerebral cortex, the cerebellum and the entire vascular system. The meningoencephalitis was of the same type as that seen in the other 3 cases.

The lesions of chronic rheumatic meningoencephalitis consist of fibrous nodular proliferations within the lumen of medium-sized and small meningeal vessels; large, polygonal, vesicular cells from the endothelium within the fibrous nodules; secondary vascularization; fibrinous exudation, frequently rich in iron; arachnoidal proliferation and nodule formation; capillary fibrosis and formation of tortuous tubules; perivascular edema and formation of fibrous webs; rather typical acellular cortical areas and granulomas, and nonspecific, but widespread, disease of the nerve cells. The vascular lesions of the meninges are associated with similar alterations in other viscera, especially the heart.

The pathologic changes of acute rheumatic encephalitis reminded Greenhill of encephalitis lethargica (a virus disease). The observations in cases of chronic rheumatic encephalitis seem, again, to support McCallum's theory that rheumatism is a virus disease or a toxic or allergic reaction. The pathologic process is different from that of syphilitic meningoencephalitis, tuberculosis or bacterial encephalitis.

Autopsies in 2 cases of torsion dystonia revealed, in addition to the lesions described in the preceding paragraphs, an increased amount of iron in the tissues of the globus pallidus. In 1 case the increase was so conspicuous that the diagnosis of Hallervorden-Spatz disease was made.

The literature on torsion dystonia reveals that a number of these cases had been recognized at autopsy as instances of hepatolenticular degeneration (Wilson's disease). Two of my cases and several reports in the literature indicate that in still other cases cirrhosis of the liver is not present but an increase in tissue iron, chiefly in the globus pallidus, suggests the diagnosis of Hallervorden-Spatz disease. The meningovascular lesions in my cases indicate, however, that the accumulation of tissue iron is a symptom, rather than a "degenerative" disease. In both my cases there was overwhelming evidence of chronic encephalitis, and the type of encephalitis suggested strongly a chronic rheumatic infection.

These observations indicate that it is not advisable to identify torsion dystonia with hepatolenticular degeneration or to establish Wilson's disease with and without cirrhosis of the liver. Designation of Wilson's disease should be reserved for hepatolenticular degeneration and should be recognized as a metabolic disorder of the brain. It is not

possible at present to decide whether there is a heredodegenerative disease of the type of Hallervorden-Spatz disease. My material suggests that at least some of these cases are instances of chronic encephalitis and that chronic rheumatic infection plays an important role.

Only in a small percentage of cases of chronic rheumatic infection does rheumatic meningoencephalitis develop. The relation between rheumatic meningoencephalitis and rheumatic infection resembles the relation of meningovascular syphilis to syphilitic infection. It is not yet known in which cases and under which conditions rheumatic encephalitis develops. One must, however, bear in mind that chorea minor is not the only manifestation of rheumatic encephalitis. Rheumatic encephalitis may occur even before the involvement of the heart is recognized. The cerebral process may result in mental retardation, pathologic behavior, "symptomatic" psychoses and epileptic seizures, or may even remain asymptomatic for a time.

Walter E. Fernald State School (78).

ACID PHOSPHATASE IN THE SENILE BRAIN

HERMAN JOSEPHY, M.D.
CHICAGO

GÖMÖRI [1] and Takamatsu [2] in 1939 showed that the presence of phosphatase can be demonstrated in tissue sections. Their work referred to alkaline phosphatase; however, later, Gömöri [3] described a method by which acid phosphatase, too, can be made visible in sections. Wolf, Kabat and Newman [4] examined the nerve tissue for acid phosphatase. They found that it contains large amounts. With proper technic, normal nerve cells, as well as nerve fibers, may give a strong positive reaction. Hard and Lassek [5] utilized the method for examination of growing axons and of degenerating nerve tissue. They found that tracts which become myelinated early exhibit enzyme activity early and that those which become myelinated late, such as the pyramidal tract, show phosphatase late. If a tract degenerates, the entire degenerating field gives a strong positive reaction for acid phosphatase. The authors discuss the possibility that the enzyme may be liberated from the degenerating axons and may play a role in the disintegration of myelin sheaths, which follows the disappearance of the neurofibrils. Bodian and Mellors [6] studied the phosphatase activity in chromatolytic nerve cells and found it greatly increased. "The increased activity is proportional to the degree of chromatolysis and is probably associated with increased nucleoprotein synthesis or degradation." Most of these studies were made on animals, that is, under optimal conditions for obtaining the material and preserving the enzyme

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From the Department of Pathology of the Chicago State Hospital.

1. Gömöri, G.: Microtechnical Demonstration of Phosphatase in Tissue Sections, Pros. Soc. Exper. Biol. & Med. **42**:23, 1939.

2. Takamatsu, H.: Histologische und biochemische Studien über die Phosphatase, Tr. Soc. path. jap. **29**:492, 1939.

3. Gömöri, G.: Distribution of Acid Phosphatase in Tissues Under Normal and Under Pathologic Conditions, Arch. Path. **32**:189 (Aug.) 1941.

4. Wolf, A.; Kabat, E. A., and Newman, W.: Histochemical Studies on Tissue Enzymes, Am. J. Path. **19**:423, 1943.

5. (*a*) Lassek, A. M., and Hard, W. L.: Acid Phosphatase in Growing Axons and Degenerating Nerve Tissue, Science **102**:123, 1945. (*b*) Hard, W. L., and Lassek, A. M.: The Pyramidal Tract: Effect of Maximal Injury on Acid Phosphatase Content in Neurons of Cats, J. Neurophysiol. **9**:121, 1946.

6. Bodian, G., and Mellors, R. C.: Phosphatase Activity in Chromatolytic Nerve Cells, Proc. Soc. Exper. Biol. & Med. **55**:243, 1943.

present in the tissue. Wolf, Kabat and Newman examined human brains and brain tumors as well.

The following report is concerned with acid phosphatase activity in senile human brains. The material was obtained at routine autopsies and was examined by the method given by Wolf, Kabat and Newman,[4] which I found to be the best of several recommended.

PRESENT INVESTIGATION

Material and Methods.—Small pieces of brain, not thicker than 2 mm., are fixed for twenty-four hours in cold acetone. The fluid is changed two or three times. The pieces are then placed in absolute alcohol and toluene, for twenty-four hours each, and are embedded in paraffin. They are left in the oven not longer than two hours. Sections are cut 10 microns thick. They are fixed to slides and deparaffinized and, after being washed for a short time in absolute alcohol and distilled water, are transferred for twenty to thirty-six hours to the following substrate, at a temperature of about 37 C.:

	Cc.
Acetate buffer *p*n 4.7	12
Lead nitrate, M/10 solution	10
Distilled water	74
Sodium glycerophosphate solution, 3.2 per cent	4

The acetate buffer which I use is made up from sodium acetate, 7 Gm.; acetic acid, 2 cc., and distilled water, 1,000 cc. I found this buffer better than the one recommended by Gömöri.[3]

If the glycerophosphate solution is added to the buffer–lead nitrate-water mixture, a white precipitate is formed immediately; it settles quickly. Evidently, it does not interfere with the phosphatase reaction. Sections incubated in the turbid substrate are as good as those which are treated with a filtered and clear mixture.

After incubation, the sections are washed for one-half hour in five or six changes of distilled water. Then they are immersed in a weak solution of yellow ammonium sulfide—about 1 cc. of the concentrated compound to 1 Coplin jar of distilled water. Here they become brown as lead sulfide is formed. They are washed in tap water and mounted in balsam. They may be counterstained. Deposits of phosphatase stain brown, from light shades to almost black.

Changes in the substrate may be made. I have tried that described by Hard and Lassek,[5] without finding any advantage in it. Addition of ascorbic acid, as proposed by these authors, apparently did not improve the results. The acid phosphatase substrate for blood chemical determinations, which was recommended by Bray,[7] with the addition of 10 per cent of tenth-molar solution of lead nitrate, works well.

Wolf, Kabat and Newman [4] stated that sections taken from the surface of the blocks give better results than those from deeper portions. Lassek and Hard [5a] found that the blocks should be worked up soon after embedding, as after some time the reaction becomes weaker or disappears completely. I can confirm both these observations. Furthermore, results are better in material obtained soon after death. However, I obtained good sections from brains removed eleven hours after death.

Sodium fluoride in a concentration as low as one thousandth molar destroys the phosphatase. Wolf, Kabat and Newman [4] suggested incubation of adjacent sec-

7. Bray, W. E.: Synopsis of Clinical Laboratory Methods, ed. 4, St. Louis, C. V. Mosby Company, 1946.

tions in two substrates: the usual substrate and the same substrate with the addition of sodium fluoride. Sections treated as usual exhibited staining which did not appear in those incubated in the substrate plus sodium fluoride. This proves that the brown impregnations actually indicate enzyme activity. Furthermore, I incubated sections in a buffer–lead nitrate mixture without sodium glycerophosphate, to make sure that positive results were not due to simple impregnation with lead. No staining was obtained.

The material which I examined was obtained from male and female patients who died in a hospital for mental diseases and whose condition was diagnosed clinically as senile dementia. All the patients were over 60 years of age. A few brains of younger persons were examined.

Observations.—The brains were divided into two groups on a neuropathologic basis: those exhibiting many senile plaques and/or many nerve cells with Alzheimer's fibrillary changes, and those not exhibiting these changes, at least not to an appreciable degree.

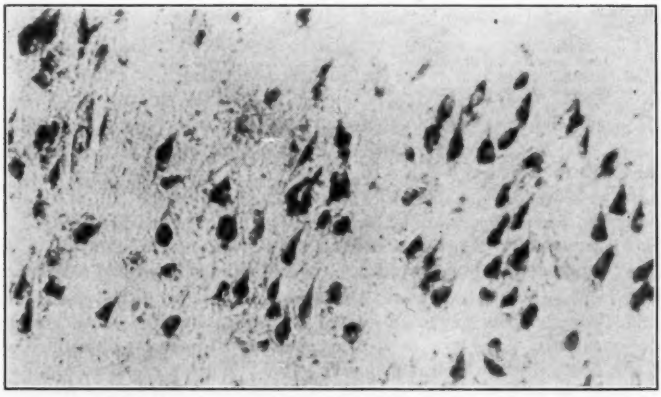

Fig. 1.—Acid phosphatase reaction of the nerve cells of the cornu ammonis of a man aged 60. Wolf, Kabat and Newman method.

In the latter group, I can confirm the results of Wolf, Kabat and Newman.[4] Nerve cells might give a strongly positive reaction. Sometimes the entire architectural structure was visible in the sections, as each cell was stained dark brown and was well outlined (fig. 1). The tissue betwen the cells took a faint brown color. In the individual cell, the nucleus and the nucleolus were stained, and the protoplasm took the stain rather diffusely. Sometimes intracellular fibrils could be distinguished. However, the lead sulfide was never distributed in the pattern of the Nissl bodies. Extracellular neurofibrils were stained too, yet seldom as completely as the cells. Apparently, there was an inverse relation between the staining of cells and that of fibers—if the cells were stained intensely, fibers were not well stained, and if the cells gave a weak reaction, fibers showed considerable phosphatase activity.

Several times I found well stained baskets around the Purkinje cells. The epithelium of the choroid plexus gave a strong reaction. In the glia, the nuclei only were stained, not the cytoplasm.

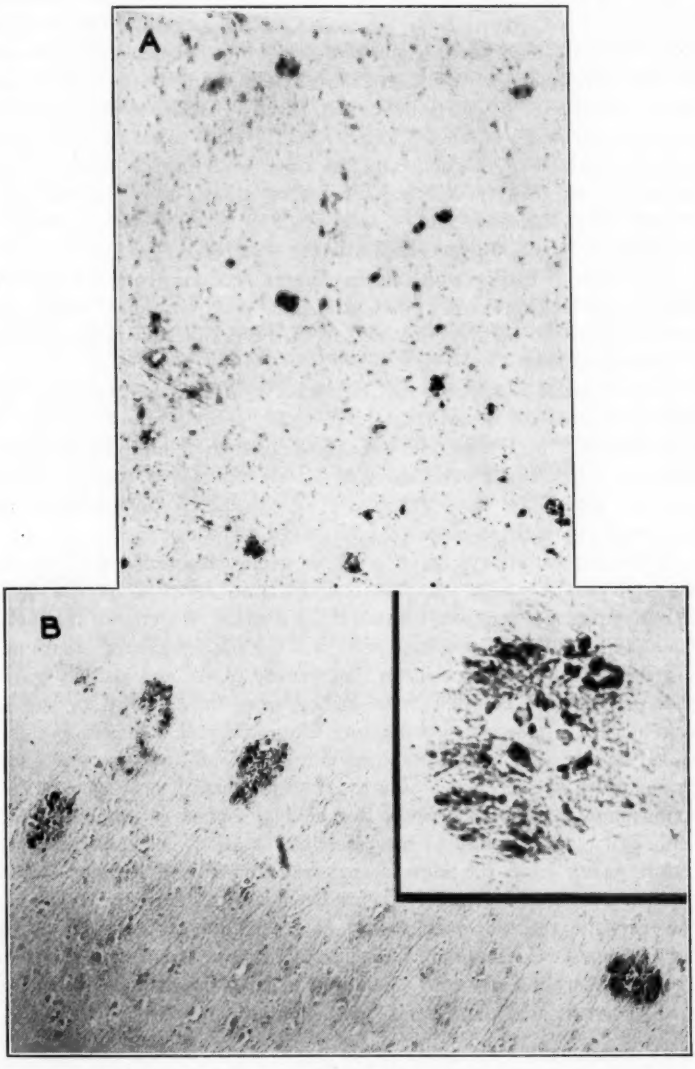

Fig. 2.—*A*, Acid phosphatase reaction. Senile plaques in the cortex of a man aged 72.

B, senile plaques in the cornu ammonis of a woman aged 80. Inset shows a plaque under high power magnification. Wolf, Kabat and Newman method.

These results obtained on the brains of old persons without plaques and/or Alzheimer's fibrils apparently are identical with those obtainable in the brains of younger persons.

It is difficult to estimate the amount of phosphatase present from the intensity of the brown color developed in the sections. Wolf, Kabat and Newman [4] have already noted this point. The reaction is weaker in the deeper layers of the paraffin blocks than in the upper ones. Therefore, if the section is not taken exactly parallel to the surface of the specimen and is cut even slightly on the bias, one side of a section may show a strong reaction, and the other end may be rather weakly stained or be entirely colorless. In other words, a very dark brown impregnation indicates intense phosphatase activity, but a weak or negative result is not always indicative of weak activity.

However, it can be said that in general sections from the brains of senile patients apparently give stronger reactions and stain more intensely than do sections obtained from the brains of younger patients without dementia.

Examination of brains with Alzheimer's fibrillary changes and with senile plaques gave a surprising, and hitherto undescribed, result (fig. 2, *A* and *B*). Senile plaques contained a large amount of acid phosphatase. They stood out clearly and well defined in sections treated with the method already described. Well stained preparations were comparable with those obtained with silver methods.

The plaques always gave a very strong reaction; that is, they appeared almost black. Higher magnification revealed all the details seen in silver preparations: amorphous masses, sometimes resembling nerve cells; fibers, and occasionally a dark-stained center surrounded by a light halo. Nerve cells in the vicinity of plaques usually gave a weak phosphatase reaction only. They were light brown or did not stain at all. In sections containing many plaques I never got them stained as intensely as those shown in figure 1. Moreover, few neurofibrils stained in such preparations. It seems that all plaques in a given section show a positive reaction for acid phosphatase; apparently, the number of plaques found in these sections is about the same as that in sections taken from the same region and stained by a silver method. In some instances I found Alzheimer's fibrils rather intensely stained. However, the reaction was neither as strong nor as constant as that of the plaques. Comparative Bielschowsky preparations showed a much larger number of cells with Alzheimer's fibrillary changes than were impregnated in acid phosphatase preparations.

COMMENT

Staining, or, better, impregnation, of nerve cells, neurofibrils and, especially, senile plaques was obtained by methods used for the demon-

stration of acid phosphatase activity in tissues. This means more than just another way to demonstrate these elements. It indicates definitely an enzyme activity, with the enzyme, the acid phosphatase, located in the parts giving a positive reaction. It can be stated that the senile plaques contain acid phosphatase.

As previously pointed out, the intensity of the phosphatase reaction as obtained in sections does not necessarily indicate quantitative variations. However, the fact that plaques always give a strong reaction and the impression that in general the nerve cells in brains of persons with senile dementia seem to stain darker than those in brains of younger, undemented persons suggest the possibility that the actual amount of phosphatase may increase with old age and with the development of senile dementia. Further studies in this direction are in progress.

The phosphatase found in the plaques and the apparently increased amount of it in senile nerve cells may indicate an increased local production of this enzyme, or an increased storage from the blood, or a shift from other elements in the nervous system to plaques and nerve cells. Some of the observations seem to favor the idea that there is a shift.

It should be noted that, in general, structures in the nervous system which take the silver stain in Bielschowsky and similar preparations give a positive reaction to the acid phosphatase test.

SUMMARY

Acid phosphatase is present in nerve cells and fibers of the senile brain, apparently in rather large amounts.

The enzyme is found regularly in senile plaques, which "stain" intensely.

Exact quantitative studies of the phosphatase content of brains at various ages are indicated.

6500 Irving Park Road (14).

EFFICACY OF THE BRIEF CLINICAL INTERVIEW METHOD IN PREDICTING ADJUSTMENTS

Five Year Follow-Up Study of Three Hundred and Four Army Inductees

JOHN A. AITA, Ph.D., M.D.
OMAHA

IN 1941 the problem of rapid psychiatric screening at the military induction center was of major concern.[1] At that time [2] it was suggested that there would be a day of reckoning and that a follow-up study would be the only means by which those endeavors could be evaluated scientifically.

Although problems of wartime mobilization are now past, it is important that one examine critically the efficacy of rapid clinical interviews in predicting adjustments. The practicing psychiatrist occasionally is expected to make a quick decision of this nature. Industry and educational systems likewise may demand rapid screening examinations to eliminate the unfit and the potentially unfit.

FOLLOW-UP STUDY

The purpose of this study is to examine the subsequent military careers of two extreme groups of men inducted into the Army in early 1941. A successful adjustment was predicted for one group; the other, containing likely failures and borderline candidates, was deemed questionable material. Rejectees were not included.

Material.—Between January and April 1941 I examined many hundreds of Army inductees at Fort Snelling, Minn. At that time brief, hurried records were compiled. In August 1946 my colleagues and I studied the wartime records of men for whom successful adjustment had been predicted and of others who, although not rejected, were considered questionable or dubious soldier material.

Criteria for these predictions have previously been explained.[3] We were governed not by set standards but by clinical impressions of more or less

1. Aita, J. A.: Problem of Neurologic and Psychiatric Examination During Military Mobilization, Proc. Staff Meet., Mayo Clin. **16**:283 (April 30); 294 (May 7); 307 (May 14) 1941.

2. Aita, J. A.: Neurologic and Psychiatric Examinations During Military Mobilization: A Review of 9,542 Examinations, War Med. **1**:769 (Nov.) 1941.

3. Neuropsychiatric Examinations of Applicants for Voluntary Enlistment and Selectees for Induction, Circular Letter Nineteen, United States War Department, Office of Surgeon General, Washington, D. C., March 12, 1941.

experienced psychiatrists. We sought the feebleminded, the paranoid and the schizophrenic; the men with the manic-depressive psychosis, the psychopathic; those with addiction to drugs or with organic disease. Without subtlety, we also searched for clues which hinted of such conditions or predispositions. As a result, in 1941 we [2] rejected for neuropsychiatric reasons 2.5 per cent of the men examined. Another 5.7 per cent, although not rejected, were considered borderline or questionable risks. These were the men whom we would have rejected had medical-military standards been stricter at the time. These were the men with potential psychoneuroses and "breakdowns." On the other hand, the man with a high school education or a steady job, who had always had good health, who appeared robust and neither unduly resentful nor fearful of military service, was usually classified as excellent soldier material.

Method.—From the many thousands of unselected records, I chose those of 250 men for whom I had predicted successful careers. Likewise the records of another 250 were taken about whom definite doubt was expressed at their induction.

In August 1946 we were able to obtain full medical and military personnel records on 304 of this group of 500 men. Reasons for the incompleteness of 196 records, carefully checked with the various branches of the Adjutant General's Department, were found to be multiple, and similar for the two groups under study. Hence deletion of these 196 records merely reduced the total number but did not introduce a new element of selection.

Medical and personnel records revealed succinct information concerning skills, promotions, overseas service, combat experience, unit and individual awards, wounds, disciplinary action, duration of service, hospitalizations, symptoms and diagnoses and mode of discharge.

Definitions.—A soldier was classified as successful if he had withstood many hardships or actively contributed to the achievements of his organization. For the purpose of this study, his record had to show (1) at least four years of continuous service, (2) overseas duty of more than two years, (3) absence of any disciplinary action and (4) minimal hospitalization except for wounds or diseases endemic to the theater of operations. In addition, men in this category had at least two of the following qualifications: the rating of sergeant or technician grade 4, more than three battle stars, such individual awards for outstanding performance as the bronze or silver star medal, a combat infantry or combat medical badge or the purple heart medal.

To be termed as having made an average adjustment, a man's final ledger of service rendered showed that he contributed somewhat more to the Army than that represented by the Army's expenditure of time and money in maintaining him. His record was good but did not contain the foregoing criteria of the successful soldier. He had usually served at least four years and had required minimal disciplinary action. Men who served well and whose initial psychiatric symptoms appeared only after two years of service were classified with this group. Men with superior records were placed in this category if their deeds were interspersed with disciplinary action. Men with satisfactory per-

formance who were discharged because of family dependents or medical reasons other than psychiatric disorders, wounds or endemic diseases were also routinely assigned to this group.

The soldier classified as a failure had sufficient evidence in his records to demonstrate that his performance added up to a liability to the service. In some cases, he had broken down with a psychiatric disorder before two years of duty. In other instances he had received an administrative discharge because of poor habits or traits of character, enuresis or inaptness. In several cases there were many courts-martial. In others, evidence of repeated and long hospitalizations for ill defined backache, headache and similar conditions had strong psychosomatic implications.

TABLE 1.—*Military Record of 150 Men for Whom the Prediction of Successful Adjustment Was Made*

	Number	Percentage
Failure	7	4.7
Average	40	26.6
Successful	103	68.6

TABLE 2.—*Military Records of 154 Men Rated as Poor Soldier Material*

	Number	Percentage
Failure	32	20.8
Average	76	49.3
Successful	46	29.9

DATA

The final outcomes for the two groups for whom predictions were made are shown in tables 1 and 2. Four times as many failures appeared among the men for whom the prediction of questionable soldier material was made in 1941 as among the group for whom success was predicted. Over twice as many successful soldiers came from the group for whom this prediction was made. However, among those rated as questionable material, for every 2 men who proved to be failures, there were 3 who became successful soldiers.

Premature Separation.—Removal of men discharged prematurely for reasons of dependency or disability (other than psychiatric disorders, wounds or endemic disease) affected the statistical impressions but little, as revealed in tables 3 and 4.

Psychiatric Casualties.—Almost three times as many psychiatric casualties came from the group given a poor outlook in 1941 as that rated as good soldier material; nor did the number of breakdowns diminish after two years of service. This is demonstrated by table 5.

It should again be emphasized that not all psychiatric casualties were classified as failures in the preceding tables, but were usually termed as making an average adjustment if the man's performance was good for at least two years. Likewise, all failures did not carry a formal psychiatric diagnosis. Many chronic disciplinary problems never received a psychiatric tag.

Service Record Details.—Other differences and details are shown in round numbers in table 6. For the most part, individual differences are not great but the consistently better record of the group for which a successful career was predicted is evident.

TABLE 3.—*Military Records of 144 Men for Whom the Prediction of Successful Adjustment Was Made and Who Were Not Prematurely Separated from the Service*

	Number	Percentage
Failure	7	4.9
Average	34	23.8
Successful	103	72.1

TABLE 4.—*Military Records of 132 Men Rated as Poor Soldiers Who Were Not Prematurely Separated from the Service*

	Number	Percentage
Failure	32	24.3
Average	54	41.0
Successful	46	35.0

TABLE 5.—*Psychiatric Casualties*

	Predicted Successful Soldiers, per Cent	Predicted Poor Soldiers, per Cent
Total	7.0	20.0
Onset of disability within 2 years' duty	4.5	7.1
Onset of disability after 2 years' duty	2.5	12.9

REVIEW OF NOTATIONS IN 1941 RECORDS

Men Rated as Poor Soldier Material Who Became Successful Soldiers.—The following representative notations were taken from the 1941 induction center examination forms for men then rated as poor risks who nevertheless became successful soldiers: (1) "nervous" gastrointestinal system; (2) many asthenic symptoms, poor CCC record with dishonorable discharge; (3) chronic weak back, alcoholism; (4) claustrophobia, tics, fear of Army life; (5) paranoid appearance, nervous breakdown at 18; (6) migraine headaches, frequent gastrointestinal upsets for past three years; (7) nervous, timid child, sexual preoccupations, neurasthenia with functional heart complaints; (8) easy irrita-

bility, frequent spells of depression and alcoholic abuse, dishonorable Civilian Conservation Corps (CCC) discharge; (9) feminine in type, "highstrung," artistic, indifferent; (10) weakness and tendency to faint easily, enuresis up to age of 17.

Men Rated as Poor Soldier Material Who Proved to be Failures.—Representative notations in 1941 follow: (1) chronic headaches, prudish, hypochondriacal; (2) anxious, asthenic, effeminate, given to use of phenobarbital; (3) artistic, "temperamental," with a history of moderately severe reactive depression eighteen months before; (4) much complaint of gastrointestinal symptoms and worry over health; (5) headaches, gastrointestinal symptoms; dull, slow, introspective; (6)

TABLE 6.—*Other Data on Service Records*

	Predicted Successful Soldiers	Predicted Poor Soldiers
Ratings	81%	50%
Corporal, technician 5th grade	20%	25%
Sergeant, technician 4th and 3d grade	61%	25%
Overseas service	94%	74%
Battle stars	70%	58%
Average number of stars	5.0	3.1
Combat badges	16%	23%
Good conduct medal	77%	57%
Purple heart	15%	12%
Individual awards (medals)	14%	2%
Unit awards	21%	10%
Court-martial	10%	10%
Average number per man	1.2	2.6
Killed in action	5%	4%
Demobilized after 4 years' service	70%	60%
Premature discharge because of dependents or medical discharge (not for psychiatric illness, wounds or endemic disease)	9%	15%

tense, recently divorced, heavy use of alcohol, chronic backaches; (7) acute anxiety attacks with cardiovascular emphasis, for three years; (8) marked tremulousness, limited intelligence quotient; (9) effeminate, periods of moderate depression; (10) reticent, nervous, many fears, recent fainting.

A detailed scrutiny of our 1941 notations in the light of the subsequent records of each man revealed no significant criteria for prediction. It appears that we had been concerned too frequently with moderate intellectual limitations and borderline educational or occupational records. Likewise, many suspected and potential psychoneurotic and psychosomatic conditions disappeared with military service.

COMMENT

The reasons for our inability to predict with practical efficacy are obvious. Our examinations were limited in every way. We were

attempting to predict on the basis of what these young men had been. We examiners had little doubt that the induction center revealed each man at his worst. There was no way of foreseeing future socioenvironmental encounters, good and bad, which would mean a great deal to young men. Perhaps, too, we overlooked their inherent resilience and adjustability and refused to believe that Army life might provide healthy living for some of them.

In early 1941, such additional adjuncts as written questionnaires, psychologic tests and social service data were not available or had not been given sufficient trial in induction centers. These were of screening value also, but it is doubtful whether any single method was outstanding in predictability. Certainly, a cross fire of several methods (including the clinical interview) would be of more value than any single approach.

Civilian groups will ask whether military service must contribute to the early breakdown of 21 per cent of borderline candidates. Line officers will inquire why they should be weighted down by induction of a group of men with a casualty rate of almost 25 per cent. Is not rejection of this entire group justifiable? It is recognized that many personalities would have broken despite military service because of civilian and home factors already at work. In a nation at war, where manpower becomes the all-important consideration, some psychologic risks must be taken. If we were able to predict that one third or one half of borderline candidates would break before two years of service, would we at the induction center even then be justified in depriving the military forces of the remaining useful soldiers? Or should we permit other screening systems during the training period to aid us in making a more efficient evaluation?

CONCLUSIONS

On the basis of a follow-up study of 100 men inducted into the Army in 1941 as questionable soldier material, 21 proved to be failures. Of 100 men for whom successful adjustment was predicted, 5 failed. Nevertheless, these studies indicate that had the 100 men who were questionable risks been rejected, the Army would have lost 49 average soldiers and 30 outstandingly successful soldiers.

A review of clinical data recorded for borderline selectees in 1941 provided no significant criteria on which one might base predictions. The practical significance of moderate intellectual limitations and borderline psychoneurotic disorders can be evaluated only after the inductee's exposure to military service.

Our experiences warrant the following suggestions: The psychiatrist should continue to have a place in the induction center, if for no other reason than to detect and reject the psychiatrically unfit. He

should record a simple psychiatric profile rating for each man he sees. Written questionnaires, social service data and psychologic laboratory procedures have their place in the induction center, but they in no way supplant the clinical interview. They remain secondary to it and serve only as useful adjuncts. Only candidates who are psychiatrically ill should be rejected. Definition of who is ill depends on the experience and judgment of the examiner or a group of examiners. The men with potential, possible psychopathy, with a suspicious and borderline state, rarely can be classified as ill. Our experiences indicate that in the doubtful case a chance is worth taking. The induction center serves only as the initial screening. The training center to follow provides a natural series of social, emotional, intellectual and physical hurdles. With commissioned and noncommissioned officers and medical officers trained in simple rules of mental hygiene, observation and recognition of personality disorders, the psychiatrist will have his hands full of screening problems. It appears that a far more efficient screening can be done at this stage than at the induction center.

FOLIE À DEUX (PSYCHOSIS OF ASSOCIATION)

EDUARD ASCHER, M.D.
BALTIMORE

REPORT OF A CASE

Mary and Dorothy, sisters, were admitted to a midwestern psychiatric observation hospital after they had been seen wandering the streets by police officers, who considered their behavior odd and unusual. On arrival the patients told the story of having lived in a Social Security shelter for the preceding three years, where they had been in the employment of the United States Government, with the special task of uncovering a conspiracy of Nazi agents who had their headquarters in the shelter. While performing their counterespionage work, they had frequent visits from high Government officials, who were personally supervising their work. As a result of their prominence, these patients were the object of envy by the treacherous women in the shelter and were threatened by them on numerous occasions. Eventually, the situation became so dangerous that the Government was forced to close the shelter, resulting in the patients' homelessness. While waiting for Government orders as to where to proceed, they were apprehended by the police, who had brought them to "an insane asylum, contrary to all promises." This is part of the intial story as told by the patients.

When the sisters first arrived at the hospital, the most striking feature about them was their physical appearance and the way in which they presented the delusional material. Mary, aged 52, was dressed in an old-fashioned feminine garment indicative of past prosperity. She was well groomed, with her hair drawn loosely over her forehead; she wore lipstick and rouge, her long finger nails were bright with loud, red polish. The patient's nose was pointed and quite prominent.

Dorothy, aged 47, although having somewhat different facial features, looked much like her older sister in other respects. Her hair-do was almost a likeness and so were her posture, inflection of voice and garment: she also wore lipstick, rouge and nail polish, but on her it was less noticeable.

When the patients replied to a question, the older sister always started to answer it first, in a self-assured, monotonous, deep voice, while Dorothy repeated word for word in an echo-like fashion, speaking in a high-pitched, squeaky voice. Both patients presented the delusional material in identical words, even when interviewed apart from each other.

Most of the history was obtained from friends of the family and former students of the patients' father.

Mary was the second child of then wealthy parents. Both her grandfathers were Protestant ministers. Her father, a doctor of medicine and doctor of pharmacy, was one of the most prominent citizens of the community and was greatly esteemed for his work in pharmacology and pharmacognosy. He was the founder of a midwestern college of pharmacy, where he was active until his death, of heart disease, in 1922. He had published several books on medical and pharmacologic subjects, among them one on "Phallic Worship." The latter was sensational at

From the Henry Phipps Psychiatric Clinic.

the time of its first printing, containing detailed accounts of the use by various races and religions of art objects symbolizing the phallus. In his lectures to students of pharmacology, he spent the major part of his allotted time in talking on the effects of various drugs on penile erection and ejaculation, thereby evoking considerable criticism by other faculty members. At home he was the undisputed master of the house. He undertook to give his children part of their elementary education, leaving it to private tutors to do the rest. Although he wrote several books on sexual topics, he never attempted to educate his children in that subject. The patients' mother was said to have played a subordinate role, having been confined to household duties and the like. The family standards were very high; the people with whom the children associated were carefully screened by their father, and almost all activities in which the children were permitted to take part were those arranged by their father in their own home. When the oldest child, a son, was to be married, his father rented a buggy for him which was drawn by eight horses, in order to impress the future in-laws with his "wealth." The son was also a doctor of medicine and of pharmacology, and he, too, was a member of the faculty of the aforementioned college of pharmacy. He was described by informants as having been very much like his father, both in physical appearance and in emotional makeup; he died of heart disease at the age of 35 and was said to have been the mother's favorite child and the only mentally normal member of the family.

When Mary was 20, she was married to a man 5 years her senior. She had met him in her own home during one of the social gatherings; and, after a brief courtship, she had confronted her parents with the fact that they were about to be married. The patient described her husband as having been very much like her father; he died of pulmonary tuberculosis four years after their marriage, after having spent most of the time in a sanatorium, leaving the patient with a young daughter. The latter died of a congenital heart disease when she was 4 years old.

Mary never had salaried employment. Her interests consisted of knitting and short story writing; some of the stories, which dealt with "adventure, travel, crime and romance," were published in popular magazines, according to the patient. She was never permitted to read her father's books on sexual matters and entered married life with only a scant knowledge of the subject. After her marriage she did not find sexual relations pleasant and considered them as "part of the contract she signed." In addition, the patient said, she always had a particular dislike for "sex-mad women."

Informants characterized the patient as always having been somewhat aloof, seclusive, haughty, distrustful, rigid, opinionated and of superior intelligence.

Dorothy was born five years after Mary. Her early development was said to have been normal except for the fact that she was weaned late. She was considered an obedient, well mannered child, who was shy, submissive and lacking in initiative; she was always dependent on others. Like her older sister, she was educated by private tutors, assisted by her father and sister. When 11 years old, she was severely ill with typhoid. Her older sister served as her nursemaid during that period, and subsequently Mary was the only person with whom the patient had any close relationship. Dorothy's interests were like those of her sister; she was busy writing short stories dealing with adventure, crime, romance and travel. (All the foregoing history was obtained from informants other than the patient, who was vague and evasive during interviews regarding details of her past life.) Dorothy's personality was summed up as having been impractical, dependent, passive, submissive, seclusive and indecisive, but of good intelligence.

Informants related the story that after the death of her husband and child, Mary devoted most of her time to her younger sister, Dorothy, who was then 18 years

old, and only rarely subsequent to her misfortunes did she participate in the social activities of the house. The sisters made several trips in the United States, which were sponsored by their father in order that they might collect material for their short stories.

When the patients' father died, in 1922, they began to withdraw more and more from any social contact. Only on rare occasions did they appear in public; when they did, people avoided meeting them, as they were considered queer. Their mother remained with them in the house, where they shared a life of seclusion. The large house, once the center of social life and full of splendor, became increasingly neglected. When their mother died, in 1934, the sisters were unable to maintain the home any longer, mainly for financial reasons; and when prospective buyers entered the premises they found the rooms cluttered with piles of tin cans, in addition to filth and numerous cats, which produced an almost intolerable odor. At first, the sisters found refuge in the home of a former maid, but were forced to move from there after a few years. They stayed with friends of the family for a while, but because of their odd behavior were not permitted to remain there. Eventually they were admitted to the shelter, where they continued to live a life of seclusion and appeared in public only at mealtimes; they were suspicious and refused to permit any one to enter their room. When the shelter was closed for lack of public funds, the sisters had to be ejected and were brought to the hospital after they had been seen wandering the streets aimlessly.

After the initial period in the psychiatric hospital, the patients continued to be suspicious and indignant about having to be with "insane creatures." Whatever information was obtained from them was supplied by Mary, while Dorothy was vague and frequently refused outright to talk at all. They complained bitterly that other women in the shelter had threatened to disfigure their noses, adding that they had been warned by their father on many occasions to be on guard against such a happening.

The results of physical and neurologic examinations were entirely normal. The findings in routine laboratory tests were all within the range of normal. Psychometric evaluations revealed that Mary's intelligence quotient was slightly above average, whereas Dorothy's score was average.

Several attempts to interview the sisters together were not very successful. When one of them (usually the older) was about to say something, the other interrupted by stating that they were not allowed to give any information, whereupon both, at the same time and in identical words, repeated that "they were not allowed to give any information." It was then decided to interview them separately and to start with the older one. After an initial period of suspiciousness (during which the patient considered the doctor as an "envoy of a sanatorium where she was to be put away"), she became increasingly friendly and began to talk a good deal of her past life, particularly about the splendor of the home and her father's brilliant education. It was noted that the improvement in the doctor-patient relationship with the older sister was paralleled by an equal improvement in that with the younger one, who now took pains to apologize for her unfriendly attitude during preceding interviews.

Mary complained but little about what appeared inconvenient to her in the ward, but frequently pointed out that it was "sister" who suffered. She told of pinching her sister's arm one night, only to find out that "the poor soul had been wide awake because of the intolerable noise."

When it was planned to separate and house the two sisters in different hospital wards, it was Mary who volunteered to go the noisier one, because, as she said, she was hard of hearing and could tolerate noise easier than "poor Dorothy." As

soon as the actual separation took place, Mary made a fairly good adjustment to the new environment. She talked with other patients for the first time and appeared generally somewhat more cheerful. She inquired about her younger sister frequently but did not express a strong desire to return to her. Dorothy, on the other hand, grew increasingly irritable and demanded aggressively that she be permitted to be with her sister again.

During interviews Mary at first continued to elaborate on her delusions, pointing out how endangered she felt by the women about her. As time went on, she shifted the theme of her conversation to events of the past and simultaneously became more sociable with other patients in the ward.

The interviews with Dorothy during the period of separation revealed the same delusional content, identically worded; however, the beliefs were presented somewhat more hesitatingly and not spontaneously; on many occasions the patient terminated an interview abruptly and prematurely by saying: "Give me liberty or give me death!"

While in the hospital, Dorothy had a moderately severe peritonsillar abscess on the right side of the pharynx, which necessitated surgical drainage. Four days thereafter, Mary exhibited a peritonsillar abscess in the identical region on the right side of her pharynx, resulting in considerable difficulty in speaking. It was observed that during that time Dorothy talked more freely on matters that she had refused to discuss up to that time. She also discarded the high pitch of her voice and added a delusion of her own to the effect that she had been visited in the hospital by some of her prominent friends.

The patients' behavior and condition became static after a while; when the period of observation was terminated, they were transferred to a psychiatric institution for custodial care and treatment.

COMMENT

Folie à deux, double insanity (Tuke), or psychosis of association (Gralnick [1]), according to Flournoy,[2] was first mentioned by Baillarger, but Lasègue and Falret [3] first described the disorder in detail after reporting 7 cases. There is considerable discussion in the literature concerning the etiology of folie à deux, particularly whether the mental illness is transmitted from one sick person to a healthy one, or whether it merely happens to occur in two or more people at the same time. Régis [4] introduced the term folie simultanée, or simultaneous psychosis. Marandon de Montyel [5] divided folie à deux into three separate conditions, (*a*) folie imposée, (*b*) folie simultanée and (*c*) folie communiquée, the last referring to hereditarily predisposed persons who adopt one or more delusions from others and retain them in spite of separation. Flournoy [2]

1. Gralnick, A: Folie à deux: The Psychosis of Association, Psychiatric Quart. **46**:230, 1942.

2. Flournoy, H.: Folie à deux, Schweiz. Arch. f. Neurol. u. Psychiat. **20**:44, 1927.

3. Lasègue, C., and Falret, J.: La folie à deux ou folie communiquée, Ann. med.-psychol. **18**:321, 1877.

4. Régis, cited by Flournoy.[2]

5. Marandon de Montyel, E.: Contribution à l'étude de la folie à deux, Ann. med.-psychol. **5**:28, 1881.

expressed the belief that folie imposée is not a true psychosis but a phenomenon of suggestion. He stressed the importance of the "affective relationship" between the persons, calling it a phenomenon of transference. The relative infrequency of the disorder was noted by Coleman and Last [6] and by Brussel.[7]

Kraepelin [8] stated that the mere separation of the patients in a case of folie à deux sufficed to achieve a permanent cure. Oberndorf [9] expressed the opinion that optimally the patients should be treated while still together, although separation might appear desirable. Adler and Magruder [10] reported successful treatment by electric shock after separation of the 2 patients (identical twins) had failed to produce improvement. The authors stressed the importance of the time element in treatment and advocated prompt and early therapy.

Although only about 100 cases of folie à deux are on record, it is my belief that the disorder is commoner than would appear. The 2 sisters described in this presentation probably would never have come to the attention of a psychiatrist had they either possessed sufficient funds to continue living in their home or been permitted to remain in the shelter.

The case presented differs from most others published in the unusual family background and in the fact that the delusions presented were not only similar in the 2 patients but were actually identically worded, regardless of whether the patients were together or separated.

The question arises in this case whether one is concerned with folie imposée or folie simultanée.[5] Gralnick [1] pointed out the desirability for classification within the folie à deux group. There is considerable evidence to support the opinion that Dorothy had shown signs of maladjustment throughout her entire life. Her late weaning and her passive attitudes toward people around her, aggravated by her severe illness during childhood, point toward an exaggerated and excessive need for dependence on her part. Mary, on the other hand, although she had experienced considerable frustration in the restricted atmosphere of the home, made a courageous attempt to find satisfaction in marriage, but failed to achieve her aim, as a result of her Victorian upbringing, and probably also because she identified her husband with her beloved and feared father, with resulting inability to enjoy sexual relations. In addition, she lost, in short succession, her husband, her daughter and her father, by death.

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6. Coleman, S. M., and Last, S. L.: A Study of Folie à Deux, J. Ment. Sc. **85**:1212, 1939.

7. Brussel, J. A.: Folie à Deux, Psychiatric Quart. **12**:331, 1938.

8. Kraepelin, E.: Psychiatrie, Leipzig, Johann Ambrosius Barthe, 1899, vol. 1, pp. 74-75.

9. Oberndorf, C. P.: Folie à Deux, Internat. J. Psycho-Analysis **15**:14, 1934.

10. Adler, A., and Magruder, W.: Folie à Deux in Identical Twins Treated with Electroshock Therapy, J. Nerv. & Ment. Dis. **103**:181, 1946.

It was only natural that she turned to her sister for emotional support, since the latter herself was very much in need of Mary's. With all the bitter resentments against a world that had offered her nothing but frustration and disappointments, she gradually withdrew from it more and more, in the company of her sister and mother, who at that time was probably psychotic as well (folie à trois?). When the mother died, the sisters were evicted from their home and from every other place in which they sought refuge. What was left them were the common bonds of two utterly unhappy people and the "splendor" of a past which they desperately attempted to preserve in the form of grandiose delusions. Separation of the patients proved that both continued to present delusions, thus showing evidence of psychotic illness in both sisters even when apart. On clinical observation and examination, the personality disorganization of the younger sister seemed more pronounced, an impression which was confirmed and supported by a Rorschach evaluation.

Considering the duration of the illness and the scarcity of tangible personality assets, the prospects for successful treatment in this case did not appear bright. On the other hand, since the psychiatrist had nothing better to offer, it would have been foolish indeed to deprive these 2 people of the only personal relationship that had any real meaning to them, namely, that of the one with the other. Such treatment by separation may be reserved for the occasional case of folie imposée but it certainly is not helpful in folie simultanée, as presented in the present case.

SUMMARY

1. A case of folie à deux in 2 sisters is reported which was characterized by an unusual family background and striking clinical features, including the simultaneous occurrence of an identical physical illness in the 2 patients.

2. The case is discussed with special reference to the portion of the literature which deals with classification, psychodynamics and treatment.

3. The opinion is expressed that the folie à deux relationship should be broken up by separation only in case of folie imposée or in such other cases as those in which a useful doctor-patient relationship could be substituted for an unhealthy patient-patient relationship.

Henry Phipps Psychiatric Clinic.

OPTOKINETIC RESPONSE AND INTRACRANIAL LESIONS

DAVID G. COGAN, M.D.
AND
DONALD R. LOEB, M.D.
BOSTON

DESPITE its simplicity and ease of performance, the optokinetic test is not widely used in neuro-ophthalmologic examinations, and there appears to be limited appreciation of its significance in neurologic disease. This is due, no doubt, to an insufficiency of clinical data. Accordingly, it is the purpose of the present paper to record and analyze the results obtained with the optokinetic test in a group of patients with neurologic disease.

The optokinetic response is elicited by continuously moving the visual field, or the central portion of it, in one direction. The eyes follow the objects of fixation to the limit of the field or to the limit of comfortable conjugate gaze and then make a quick corrective movement in the opposite direction. The repetition of this cycle is known as optokinetic nystagmus. It is readily and regularly elicited in all normal persons and cannot be inhibited voluntarily.

Optokinetic testing was introduced into clinical practice when Bárány [1] reported that it might be an objective method of detecting hemianopsia. Although this idea was soon found to be erroneous, since many patients with hemianopsia had normal optokinetic response and some patients with abnormal optokinetic response had no hemianopsia, Bárány's observation stimulated the subsequent clinical reports on optokinetic nystagmus. Noteworthy series of cases,[2] mostly small in

From the Howe Laboratory of Ophthalmology, Harvard Medical School and Massachusetts Eye and Ear Infirmary.

1. Bárány, R.: Zur Klinik und Theorie des Eisenbahnnystagmus, Acta otolaryng. **3**:260, 1920.

2. (*a*) Wernøe, T. B.: Eisenbahnnystagmus, Ugesk. f. læger **83**:1516, 1921; abstracted, Zentralbl. f. d. ges. Ophth. **7**:252, 1922. (*b*) Strauss, H.: Die diagnostische Bedeutung des optomotorischen (Eisenbahn-) Nystagmus für die Neurologie, Ztschr. f. d. ges. Neurol. u. Psychiat. **98**:93, 1925. (*c*) Stenvers, H. E.: Ueber den optischen Nystagmus; abstracted, Zentralbl. f. d. ges. Ophth. **15**:427, 1926. (*d*) Cords, R.: Optisch-motorisches Feld und optisch-motorische Bahn. Ein Beitrag zur Physiologie und Pathologie der Rindeninnervation der Augenmuskeln, Arch. f. Ophth. **117**:58, 1926. (*e*) Fox, J. C., and Holmes, G.: Optic Nystagmus and Its Value in the Localization of Cerebral Lesions, Brain **49**:333, 1926. (*f*) Fox, J. C., Jr.: Disorders of Optic Nystagmus Due to Cerebral

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number and totaling not more than 200, which show the potential relation between disturbances of the optokinetic response and intracranial disease have been reported. The reports have been concerned almost exclusively with cerebral lesions and may be summed up by the observation that lasting disturbances in the optokinetic response are especially characteristic of lesions in the posterior half of the cerebrum. The present study was undertaken to determine the validity of these conclusions.

TECHNIC AND MATERIAL

To elicit the optokinetic response, a rotating drum was used. This consisted of a tin cylinder 8 inches (20 cm.) in diameter, pivoted on an axial rod held in the hand. Black figures, approximately 3 inches (7.5 cm.) in height, of diamonds, hearts, clubs and spades pasted on the white outer covering of the cylinder served to attract the patient's attention and hold fixation. The drum, held at distances of 1 to 2 feet (30 to 60 cm.), was rotated so as to produce movements of the eyes horizontally at varying speeds. The direction of rotation was designated according to how the patient saw the field move. The optokinetic response was interpreted as abnormal when, on rotation of the drum in the two directions, there was a difference in response that was grossly evident and constantly present. This difference varied from a poorly sustained nystagmus to absence of nystagmus on rotation of the drum in one direction as compared with that in the opposite direction. Also considered as cases of abnormal response were those in which, despite alertness on the part of the patient, no optokinetic response could be elicited in either direction.

The patients making up the present series were not selected on any basis other than that they were known to have intracranial lesions, including vascular lesions, abscesses, tumors, injuries and, in 1 case, a tuberculoma. Not included in the series were patients whom it was impossible to test because of blindness or stupor or in whom the lesion could not be localized. For the analysis of the findings, the patients were grouped according to the situation of the lesion in one of the main subdivisions of the brain and, in the case of the cerebrum, in the anterior, middle or posterior portion. In addition, a division is included in which the evidence indicated involvement of most or all of one cerebral hemisphere or all of its efferent pathways. Localization was made by necropsy or operation or by the association of indisputable signs and symptoms.

RESULTS

The results obtained in patients with cerebral lesions were considered most significant and will be described first. Some of the findings are presented in table 1, arranged according to the portion of the cere-

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Tumors, Arch. Neurol. & Psychiat. **28**:1007 (Nov.) 1932. (*g*) Kestenbaum, A.: Zur Klinik des optokinetischen Nystagmus, Arch. f. Ophth. **124**:339, 1930. (*h*) Strauss, H.: Ueber die hirnlokalisatorische Bedeutung des einseitigen Ausfalls des optokinetischen Nystagmus und der hemianopischen Aufmerksamkeitsschwache, Ztschr. f. d. ges. Neurol. u. Psychiat. **143**:427, 1933. (*i*) Lenz: Das Verhalten des optokinetic Nystagmus bie einigen Fallen von Lappenresektionen, Nervenarzt. **14**:124, 1941. (*j*) Kestenbaum, A.: Clinical Methods of Neuro-Ophthalmologic Examination, New York, Grune & Stratton, Inc., 1946.

brum in which the lesion was situated. Abnormalities of the optokinetic response are seen to have been present predominantly with lesions of the posterior or middle portion of the brain, but it is noteworthy that the response may be abnormal with lesions which, so far as we could ascertain, were situated exclusively in the anterior portion of the cerebrum. It is also noteworthy, since statements have been made to the contrary, that lesions in the middle or parietal portion of the brain may be present without resulting in an abnormality of the optokinetic response.

When abnormal, the optokinetic response was deficient when the drum was rotated toward the side of the lesion. For the 1 exception to this rule noted in table 1 we have no explanation unless it was an error in the initial recording of the data.

TABLE 1.—*Correlation of Site of Lesion with Optokinetic Response in a Series of Patients with Unilateral Cerebral Disease*

Site of Lesion in Cerebrum *	Number of Patients Showing Abnormal Optokinetic Response When Drum Is Rotated So That Visual Field Moves Toward Side of Lesion	Number of Patients Showing Abnormal Optokinetic Response When Drum Is Rotated So That Visual Field Moves Toward Side Opposite Lesion	Number of Patients Showing No Abnormality of Optokinetic Response
Anterior	2	0	19
Middle	32	1	6
Posterior	10	0	2
Whole	13	0	5

* Anterior cerebral lesions are those in the frontal region; middle cerebral lesions are those in the frontotemporal, temporal or parietal region; posterior cerebral lesions are those in the parieto-occipital or occipital region, and whole cerebral lesions are those involving most of one cerebral hemisphere or its efferent pathways.

Not recorded in table 1 are 6 cases of bilateral cerebral lesions, in 3 of which the lesion was believed to involve much of both cerebral hemispheres, in 2 the midzone of both hemispheres and in 1 the posterior zone of both hemispheres. In all 6 cases there was either a bilateral deficiency or a bilateral absence of the optokinetic response.

Several signs and symptoms have been described in the literature with abnormalities of the optokinetic response, comprising syndromes incorporating motor aphasia,[3] astereognosis[4] and conjugate lateral

3. Wernøe:[2a] Ueber die Bedeutung des Thalamus opticus als zentraler sensorischer Einstellungsapparat sowie als Durchgangslied der Willensbahnen, besonders derjenigen Bahnen, deren Abbrechung die motorische Aphasie bedingt, Bibliot. f. læger **114**:29 and 69, 1922; abstracted, Zentralbl. f. d. ges. Ophth. **8**:248, 1923. Ohm, J.: Optokinetischer Nystagmus und Nystagmographie im Dienste der Hirndiagnostik, Arch. f. Augenh. **106**:185, 1932; Ueber die Beziehungen zwischen motorische Sprachlähmung und optokinetischen Nystagmus, Deutsche Ztschr. f. Nervenh. **154**:237, 1943.

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deviation of the eyes with closure of the lids.[5] Accordingly, we have listed in table 2 some of the prominent associated signs and symptoms noted in our cases. The data in the table are self explanatory, but the relation to hemianopsia is especially noteworthy because of the prevalent belief that abnormalities of the optokinetic response are associated with involvement of the visual pathways. Of the 58 patients in whom the optokinetic response was definitely abnormal, only 36 were shown to have hemianopsia, 18 had no hemianopsia and 4 had no study of the fields. Not evident from table 2 are the observations that in 26 of the 58 patients the asymmetric optokinetic response was the sole ocular motor abnormality, in 6 additional patients it was the only ocular motor abnormality other than deviation of the eyes with closure

TABLE 2.—*Frequency of Signs and Symptoms in a Series of 58 Patients with Unilateral Cerebral Disease Who Gave an Abnormal Optokinetic Response*

	Site of Lesion and Number of Patients *			
	Anterior Cerebral (2 Patients)	Middle Cerebral (33 Patients)	Posterior Cerebral (10 Patients)	Whole Cerebral (13 Patients)
Homonymous field defect	..	22	8	6
Hemiparesis or hemiplegia	1	18	4	12
Nystagmus	..	9	1	3
Conjugate lateral deviation of eyes with closure of lids	..	5	2	3
Alexia	..	6	..	..
Motor aphasia	..	7	0	..
Astereognosis	..	2	2	..

* The criteria for localization are presented in the footnote to table 1.

of the lids and in 9 patients it was the only abnormality in either the ocular motor or the ocular sensory system.

The optokinetic response was also examined in patients with lesions of the brain stem, cerebellum and cerebellopontile angle. The abnormality of the response, when present, was sometimes directed toward the side of the assumed lesion, sometimes toward the opposite side

4. Schott, E.: Ueber die Verwendbarkeit des Symptoms der Stereoagnosie in der topischen Diagnostik, Deutsche Ztschr. f. Nervenh. **80**:357, 1924. Marcus, A.: Untersuchungen über den Ausfall der optomotorischen Nystagmusreaktion bei Nervenerkrankungen, Dissert. Cologne, 1924. Stenvers, H. W.: Ueber die klinische Bedeutung des optischen Nystagmus für die cerebrale Diagnostik, Schweiz. Arch. f. Neurol. u. Psychiat. **14**:279, 1924; abstracted, Zentralbl. f. d. ges. Ophth. **13**:261, 1925. Fox, J. C., and Holmes, G.: Optic Nystagmus and Its Value in the Localization of Cerebral Lesions, Brain **49**:333, 1926. Cords, R., and Nolzen, L.: Weitere Untersuchungen über den optokinetischen (optomotorischen) Nystagmus, Arch. f. Ophth. **120**:506, 1928.

5. Cogan, D. G.: Neurologic Significance of Lateral Conjugate Deviation of the Eyes on Forced Closure of the Lids, Arch. Ophth. **39**:37 (Jan.) 1948.

and sometimes toward either side. This variability, together with the fact that most lesions in these regions cannot be strictly lateralized, led us to conclude that the optokinetic response has little practical value in localizing lesions in the brain stem, cerebellum or cerebellopontile angle.

COMMENT

In this, one of the largest series of cases to have been reported in which the optokinetic response has been studied, the results confirm in the main the conclusions of other investigators and point to the test as being a valuable adjunct to neuro-ophthalmologic examination. The value of the sign is emphasized by the fact that in the present series it was the only ocular motor abnormality in a large percentage of patients with cerebral lesions. Abnormalities in the response are not dependent on involvement of the visual pathway, although lesions in the posterior or middle portion of the cerebrum are the ones most apt to alter the optokinetic response.

That the optokinetic response should be abnormal on rotation of the drum toward the side of the lesion is curious in view of the cerebral representation of ocular movements to the opposite side. We have no explanation of this seeming inconsistency.

SUMMARY

In a series of 90 patients with cerebral disease the optokinetic response was abnormal in 58. With 1 possible exception, the optokinetic response was defective on rotation of the drum to the side of the lesion. It was the only ocular motor abnormality in 26 patients and the only abnormality in the ocular motor or ocular sensory system in 9 patients. Abnormality in the optokinetic response was most frequent with lesions in the posterior or the middle portion of the cerebrum, but was also found on occasion with lesions in the anterior portion of the cerebrum. It was not dependent on involvement of the visual pathways. It was found associated with other signs, in the following order: homonymous field defect, hemiparesis, nystagmus, deviation of eyes with closure of lids, alexia, motor aphasia and astereognosis. It is concluded that an abnormality in the optokinetic response is a frequent and valuable sign in the localization of cerebral disease.

In contrast to its reliability in connection with cerebral lesions, abnormalities of the optokinetic response were found to have no constant relation to the lateralization of lesions in the brain stem, cerebellum or cerebellopontile angle.

243 Charles Street (14).

EFFECTS OF ELECTROCONVULSIVE THERAPY ON DIURETIC RESPONSE TO WATER IN PSYCHOTIC PATIENTS

M. D. ALTSCHULE, M.D.
AND
K. J. TILLOTSON, M.D.
WAVERLEY, MASS.

OTHER work from this laboratory has shown that water retention occurs in association with the rapid gain in weight shown by patients who improve during the course of electroshock therapy.[1] It is known that stimulation of the posterior lobe of the pituitary gland consequent to hemoconcentration or to severe muscular effort, both of which occur during electrically induced convulsions, may cause liberation of antidiuretic hormones.[2] It is likewise known that the effects of steroid hormones also result in salt and water retention[3]; the action of these hormones is apparently increased during electroshock therapy.[4] Since it is well established that hormones of the posterior lobe of the pituitary gland inhibit water diuresis, it was considered that a study of the diuretic response to water before and after electroshock therapy might help in the evaluation of the possible role of hormonal factors in causing the changes in water content of the tissues which result from this treatment.

MATERIAL AND METHODS

Sixteen patients, ranging in age from 19 to 73 years of age, were studied; 10 were women. The diagnoses varied (table).

From the Clinical Services and the Laboratory of Clinical Physiology, McLean Hospital, Waverley, Mass., and the Departments of Medicine and Psychiatry, Harvard Medical School.

1. Altschule, M.D.; Ascoli, I., and Tillotson, K. J.: Changes in Extracellular Fluid and Plasma Volumes During the Course of Electroshock Therapy. Arch. Neurol. & Psychiat., to be published.

2. Pickford, M.: Control of the Secretion of Antidiuretic Hormone from the Pars Nervosa of the Pituitary Gland, Physiol. Rev. **25**:573, 1945.

3. Peters, J. P.: Water Exchange, Physiol. Rev. **24**:491, 1944.

4. Hoagland, H.; Malamud, W.; Kaufman, J. C., and Pincus, G.: Changes in the Electroencephalogram and in the Excretion of 17-Ketosteroids Accompanying Electroshock Therapy of Agitated Depression, Psychosom. Med. **8**:246, 1946. Altschule, M. D.; Altschule, L. H., and Tillotson, K. J.: Changes in Blood Leukocytes in Man After Electrically Induced Convulsions, to be published. Altschule, M. D., and Tillotson, K. J.: To be published.

All observations were made with the patients in the postabsorptive state. In order to avoid the effect of upright posture and of activity in diminishing diuresis, the patients were kept at rest in bed; similarly, extremes in environmental temperature were avoided. The patients voided at 7 a. m. and were then given 1,500 cc. of water, to be taken in not over twenty minutes; the same amount was given to each patient without consideration for body weight, since

Diuretic Indexes for Patients with Various Types of Psychoses Before and After Electroconvulsive Therapy

Case No.	Age, Yr.	Sex	Diagnosis	Diuresis Index	Comments
1	63	M	Manic-depressive psychosis, depressed phase	0.63 1.07	Before treatment 1 day after 4th treatment
2	63	M	Manic-depressive psychosis, depressed phase	0.73 0.97	Before treatment 1 day after 5th treatment
3	48	M	Manic-depressive psychosis, depressed phase	0.97 1.22 1.23	Before treatment 1 day after 4th treatment 1 day after 9th treatment
4	54	M	Manic-depressive psychosis, depressed phase	0.48 0.75	Before treatment 1 day after 10th treatment
5	53	F	Manic-depressive psychosis, depressed phase	1.05 0.92	Before treatment 1 day after 5th treatment
6	38	M	Psychoneurosis, reactive depression	0.90 1.05 1.00 0.77	Before treatment 1 day after 5th treatment 1 day after 11th treatment Relapse
7	28	F	Psychoneurosis, reactive depression	0.67 0.65	Before treatment 1 day after 10th treatment
8	61	F	Involutional psychosis, melancholia	1.07 1.23 1.20	Before treatment 1 day after 2d treatment 1 day after 4th treatment
9	59	F	Involutional psychosis, melancholia	0.75 0.69 0.84 0.89	Before treatment 1 day after 6th treatment 1 day after 9th treatment 4 days after 14th treatment
10	59	F	Involutional psychosis, melancholia	1.00 1.03 1.10	Before treatment 1 day after 4th treatment 1 day after 6th treatment
11	73	F	Involutional psychosis, melancholia	0.94 0.79	7 days after 15th treatment Relapse
12	30	F	Schizoaffective disorder	1.27 1.12 1.12	Before treatment 2 days after 6th treatment 8 days after 9th treatment
13	45	F	Schizophrenia, paranoid type	0.55-0.49 1.19	Before treatment 1 day after 4th treatment
14	44	F	Schizophrenia, paranoid type	1.21 1.41	Before treatment 1 day after 8th treatment
15	49	F	Schizophrenia, paranoid type	1.05 1.18 1.08	Before treatment 2 days after 4th treatment 3 days after 16th treatment
16	19	M	Schizophrenia, catatonic type	1.00 1.20 1.22	Before treatment 1 day after 2d treatment 1 day after 4th treatment

all had lost variable amounts of weight and there were no data to indicate whether normal weight, ideal weight or actual weight should be used as a basis for calculation. All urine voided spontaneously between the time the water was drunk and five hours later was measured.

For purposes of comparison, the curve for urine volume was plotted, and the amount calculated to have been formed in three hours was estimated (charts 1 and 2). This volume divided by the volume of water drunk is referred to in

the present study as the diuresis index. Normally all the water taken is excreted in the urine in three hours[5]; i.e., the diuresis index is approximately 1.0. The range of normal variation in studies made here was 0.85 to 1.15.

OBSERVATIONS

For 7 of the patients not yet treated the diuresis index was between 0.85 and 1.15, i. e., in the normal range; these subjects included 5 depressed patients and 2 patients with schizophrenia. The index was below 0.85 for 7 patients who had not yet been treated or who were in relapse, including 4 for whom it was below 0.70; 6 of the 7 patients had depressions and 1 had paranoid schizophrenia. The index was above 1.15 for only 2 untreated patients, 1 with paranoid schizophrenia

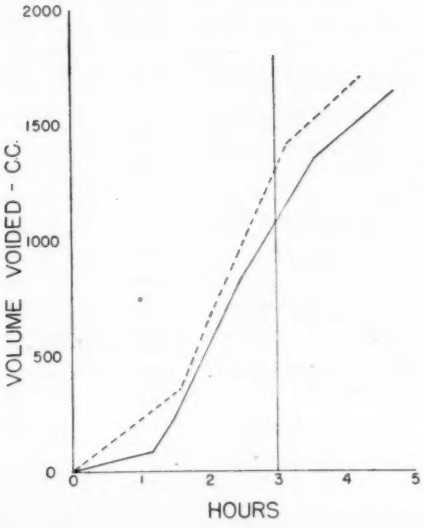

Fig. 1.—Diuresis curves for a patient (case 2) in the depressed phase of a manic-depressive psychosis. The solid line indicates the test made before, and the dotted line the test made after, a course of electroconvulsive therapy.

(case 14) and 1 with a complicated picture which was diagnosed as a schizoaffective disorder (case 12).

The shape of the curve for water diuresis was unusual in 5 patients (cases 8, 12, 14, 15 and 16) in that the usual sigmoid form was absent (chart 2); in addition, these 5 patients responded to the ingestion of 1,500 cc. of water with the excretion in five hours of 1,900 to 2,500 cc. of urine, instead of the usual 1,600 to 1,800 cc. Three of these 5 patients (cases 14, 15 and 16) had schizophrenia; another (case 8) involutional

5. Adolph, E. A.: Water Metabolism, in Luck, J. M.: Annual Review of Physiology, Stanford University, Calif., Annual Reviews, Inc., 1947, vol. 9, p. 381.

melancholia with hallucinations and delusions, and the fifth was the aforementioned patient (case 12) with a schizoaffective disorder. On the other hand, a patient with paranoid schizophrenic and another with involutional melancholia with hallucinations and delusions had curves for water excretion of the usual shape.

During the course of shock therapy a gain in weight and an increase in the diuresis index occurred in all but 3 of the patients; the 3 patients (cases 5, 7 and 12) who gained no weight during the period of study showed no increase in the diuresis index.

COMMENT

Interpretation of the nature of the changes here observed depends in part on an understanding of the characteristics of water metabolism in

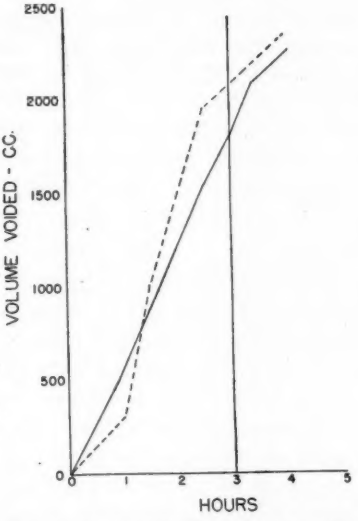

Fig. 2.—Diuresis curves for a patient (case 14) with schizophrenia. The solid line indicates the test made before, and the dotted line the test made after, a course of electroconvulsive therapy.

psychotic patients in general. For decades, reduced output of urine has been known to occur in greatly depressed patients, and Hoff and Pötzl [6] in 1930 showed that water diuresis may be inhibited in patients in the depressed phase of the manic-depressive psychosis; the later observations of Thorvardsen [7] and those of the present study confirm this finding,

6. Hoff, H., and Pötzl, O.: Untersuchungen über den Wasserhaushalt bei periodischen Psychosen, Ztschr. f. d. ges. Neurol. u Psychiat. **124**:200, 1930.

7. Thorvardsen, K.: Wasserbelastungsversuche an Melancholikern, Acta psychiat. et neurol. **17**:89, 1942.

although most of the patients here studied were probably not as severely depressed as those studied by the other authors. Hoff and Pötzl [6] further demonstrated relative unresponsiveness to xanthine and mercurial diuretic drugs in their depressed patients. Thorvardsen [7] expressed the opinion that these changes were the consequence of an antecedent decreased water intake, since in several cases he was able to demonstrate an increased diuretic response to ingestion of water in depressed patients after a preliminary period of forced fluid intake. It is, however, not valid to ascribe the retarded water diuresis seen in cases of depressions simply to deprivation of water. Thus, only 3 of the depressed patients of the present study showed specific gravities of the urine above 1.020 in a majority of casual specimens. The simultaneous occurrence of retarded water diuresis and of a normal specific gravity of the urine is suggestive of salt depletion,[8] but additional study will be required to elucidate this matter. On the basis of data now at hand, it appears that patients with depressions may have diuretic responses to water which may be normal but usually are diminished; the cause for the deviations from the normal is not established.

Water metabolism in schizophrenia is equally poorly understood. It was known previously that polyuria is common in that disorder,[9] and the present study reveals the occurrence of a rapid onset and excessive degree of diuresis after the ingestion of water. These changes are not specific for schizophrenia, for 1 of the 5 patients with schizophrenic syndromes studied here did not exhibit such effects, whereas they were shown by a patient without this disorder. The mechanism of this change in water metabolism is not known, but it resembles alteration caused by epinephrine [5]; however, the patients here studied who showed it exhibited no hypertension. The abnormalities in diuretic response observed in cases of the various psychoses were not found with sufficient regularity to make them valuable as diagnostic tests.

Gain in weight associated with water retention is the usual occurrence in patients who improve during the course of electroshock therapy.[1] Trolle [10] also noted a decrease in urinary output in depressed patients who gained weight while receiving shock therapy; however, these data by themselves are difficult to interpret, since no account was taken of other sources of loss of water. Persistent retention of water may be associated with a variety of endocrine and nonendocrine disorders. The

8. McCance, R. A.: Medical Problems in Mineral Metabolism: III. Experimental Human Salt Deficiency, Lancet **1**:823, 1936.

9. Hoskins, R. G.: Schizophrenia from the Physiological Point of View, Ann. Int. Med. **7**:445, 1933. Sleeper, F. H.: Investigation of Polyuria in Schizophrenia, Am. J. Psychiat. **91**:1019, 1935.

10. Trolle, C.: Studies of the Water Excretion in Recovery from Manic-Depressive Psychosis (Depressive Phase), Acta psychiat. et neurol. **20**:235, 1945.

former include the action of hormones of the posterior lobe of the pituitary gland, which cause water retention primarily, and of steroid hormones, which give rise to water retention as a secondary consequence of changes in electrolyte balance. It was considered that if the water retention which occurs in patients receiving electroshock therapy were due to increased secretion of hormone of the posterior lobe of the pituitary gland, water diuresis should be depressed, with a consequent fall in the diuresis index, as calculated in the present study. The diuresis index does not decrease, however, and indeed usually increases in patients who gain weight during the course of electroshock therapy. It is of interest that patients who recover from depressive episodes spontaneously also show an increased diuretic response to water.[6] In all the patients who had a high diuresis index or who showed rapidly rising diuresis curves, together with excessive polyuria before treatment, the effect of electroconvulsive therapy was the same as that in the other patients here described; i. e., the diuresis index rose.

It is clear therefore that the diuretic response to water, frequently abnormal in psychotic patients, is influenced by electroconvulsive therapy; acceleration of water diuresis is the rule. The mechanisms which regulate water metabolism in psychotic patients before and after convulsive therapy are not understood, but it appears that the water retention which occurs when convulsions are induced repeatedly is not caused by an increase in circulating hormone of the posterior lobe of the pituitary gland. It should not be concluded, however, that stimulation of the posterior lobe of the pituitary gland does not occur at all as a consequence of electroshock therapy; the present data show only that if such stimulation of the posterior lobe does occur it is not sufficient to result in retardation of the diuretic response to water.

SUMMARY AND CONCLUSIONS

The diuretic response to water has been studied in patients with various types of psychoses before and, again, after electroconvulsive therapy. Depressed patients who had not been treated or who were in relapse might show retarded diuresis after the ingestion of water, and patients with schizophrenic syndromes might exhibit abnormally accelerated and excessive diuretic responses. The abnormalities were not found with sufficient regularity to be used as diagnostic tests. After electroconvulsive therapy the diuretic response to water was accelerated in all patients who gained weight as a result of treatment and was not accelerated in those whose weight was unchanged. It is concluded that the gain in weight previously shown to be associated with retention of water is not a consequence of increased activity of antidiuretic substances.

TETRAETHYLAMMONIUM CHLORIDE IN TREATMENT OF HERPES ZOSTER AND INTERCOSTAL NEURALGIA

RALPH LEE FISHER, M.D.
MORRIS ZUKERMAN, M.D.
AND
DONALD N. SWEENY Jr., M.D.
DETROIT

THE TETRAETHYLAMMONIUM ion [1] has been established as an effective therapeutic agent in the treatment of herpes zoster and related painful conditions. Tetraethylammonium is a quarternary ammonium ion, the chloride compound of which has a structure similar to that of acetylcholine. The chief effect of the tetraethylammonium ion has been its ability to produce a block of the autonomic ganglia.[2]

Findley and Patzer [3] reported 4 cases of herpes zoster treated successfully by paravertebral procaine block. An acute inflammation of the dorsal spinal ganglia with degenerative changes in the corresponding sensory nerves, posterior horn cells and dorsal roots has been demonstrated in this disease.[4] Bielschowsky [5] has found minor inflammatory changes in the sympathetic chain at the time of an attack of herpes zoster. Vasospasm, which is a contributory factor in herpes zoster, was relieved by block of the autonomic ganglia.[3] After paravertebral procaine block, there occurs vascular dilatation with resultant hyperemia, and pain is relieved and healing of the cutaneous lesions is enhanced.

From the Departments of Internal Medicine and Surgery, Riverside Clinic.

1. Tetraethylammonium was supplied as "etamon" through the courtesy of Dr. E. A. Sharp, of Parke, Davis and Company, Detroit.

2. Acheson, G. H., and Moe, G. K.: Some Effects of Tetraethylammonium on the Mammalian Heart, J. Pharmacol. & Exper. Therap. **84**:189, 1945; Action of Tetraethylammonium Ion on the Mammalian Circulation, ibid. **87**:220, 1946. Lyons, R. H.; Moe, G. K.; Campbell, K. N.; Neligh, R. B.; Hoobler, S. W.; Berry, R. L., and Rennick, B. R.: The Effects of Blockade of the Autonomic Ganglia in Man: Preliminary Observations on the Use of Tetraethylammonium Bromide, Univ. Hosp. Bull., Ann Arbor, Mich. **12**:33, 1946; The Effects of Blockade of the Autonomic Ganglia in Man with Tetraethylammonium: Preliminary Observations on Its Clinical Application, Am. J. M. Sc. **213**:315, 1947.

3. Findley, T., and Patzer, R.: The Treatment of Herpes Zoster by Paravertebral Procaine Block, J. A. M. A. **128**:1217 (Aug. 25) 1945.

4. Head and Campbell, cited by Findley and Patzer.[3]

5. Bielschowsky, cited by Findley and Patzer.[3]

Coller and associates [6] reported the treatment of 9 patients, 5 of whom had postherpetic neuralgia of long standing and 4 acute or subacute herpes zoster. These patients were given tetraethylammonium chloride, and all patients obtained some degree of relief from pain, which varied from a brief period to six hours each time the drug was administered. The most gratifying results were obtained in the younger age group and in those patients who had acute or subacute herpes zoster. Patients with postherpetic neuralgia of long standing or with herpes of the cranial nerves noted the shortest intervals of freedom from pain.

We wish to present 4 cases in which the clinical response to tetraethylammonium chloride was excellent. In cases 1, 2 and 4 clinical symptoms and findings of herpes zoster were presented while in case 3 there were symptoms of intercostal neuralgia.

REPORT OF CASES

CASE 1.—A white woman aged 66 was first seen in the outpatient department on April 1, 1947. Four weeks previously she had severe pain of the right lower portion of the chest, followed in forty-eight hours by blisters, which formed a band around the lower right side of the thorax.

When the patient was first examined in the outpatient department, she still complained of continuous pain. Her past history was noncontributory. Physical examination revealed an obese white woman who was acutely ill. Her temperature, pulse and respiration were normal, and her blood pressure was 110 systolic and 64 diastolic. There was an area, 10 cm. in width, of crusted dermatitis of the right lower part of the thorax, which extended from the midline anteriorly to the midline posteriorly. The rest of the physical findings were within the limits of normal.

Roentgenograms of the chest and the thoracic portion of the spine showed a normal condition. A multiple lead electrocardiogram was interpreted as normal. The urine was normal and the Kahn and Kline tests gave negative reactions. The hemoglobin concentration and the red cell, white cell and differential counts were normal. The sedimentation rate was 27 mm. in sixty minutes (normal, 0 to 20 mm. in one hour). The final diagnosis was herpes zoster.

On April 4 the patient was hospitalized and was given 50 mg. of tetraethylammonium chloride intramuscularly, with the complete relief of pain within one minute. She was free of pain for six hours. Because of the return of severe pain, it was decided to give 50 mg. of this drug in the morning and at bedtime. On April 9 the patient experienced her first painless night since the onset of her illness.

After the morning injection on April 10 it was observed that the patient had relief for a period of nineteen hours and her general condition was greatly improved. The following day the eschar had disappeared, and an underlying pigmented area was noticed. From April 10 until she was discharged from the hospital, on April 30, she was given 50 mg. of tetraethylammonium chloride daily. A recent report from her family physician stated that the patient was experiencing so little discomfort that further therapy with this drug was not indicated.

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6. Coller, F. A.; Campbell, K. N.; Berry, R. E. L.; Sutler, M. R.; Lyons, R. H., and Moe, G. K.: Tetraethylammonium as an Adjunct in the Treatment of Peripheral Vascular Disease and Other Painful States, Ann. Surg. **125**:729, 1947.

CASE 2.—A white woman aged 56 was first seen on June 13, 1947, complaining of an aching pain over the right scapula, which radiated into the right axilla. This pain became progressively worse and was frequently associated with nausea and vomiting. The patient was given meperidine hydrochloride ("demerol"; isonipecaine) orally in 100 mg. doses but did not obtain relief for more than fifteen minutes. On June 16, she complained of a rash on the right side of her back and chest.

The past history revealed that she had had a spinal fusion five years previously for spondylolisthesis. Physical examination revealed that she was acutely ill. There was a vesicular rash over the right side of the chest posteriorly, extending from the fifth to the seventh rib. The rash did not cross the midline posteriorly, and several areas were noted just anterior to the axilla. The fundi revealed grade 2 narrowing of the arteries. The left border of the heart was 2 cm. beyond the midclavicular line, and the blood pressure was 245 systolic and 140 diastolic. The back revealed a linear scar over the lumbosacral articulation, where the motion was limited. Roentgenograms of the chest and the right shoulder revealed a slight enlargement of the left ventricle but no abnormality of the right shoulder. A roentgenogram of the spine revealed an old healed operative fusion of the lumbosacral articulation. There was osteoarthritis of the lumbar and thoracic portions of the spine.

The urine was normal, and the Kahn and Kline reactions were negative. The hemoglobin concentration and red cell, white cell and differential counts were within normal limits. The final diagnosis was herpes zoster and hypertension.

On June 16, 1947, the patient was given 200 mg. of tetraethylammonium chloride intravenously, with complete relief of pain, nausea and hyperesthesia in fifteen minutes. She felt well for two hours, when there was a gradual return of pain. Four hours after the initial injection she was given 200 mg. of this drug intramuscularly. In twenty-five minutes she was relieved of her pain. On June 17 the patient was given 150 mg. of tetraethylammonium chloride intramuscularly, with alleviation of symptoms for five to eight hours. The last dose was continued daily for one month. From July 17 to August 4 it was found necessary to administer 200 mg. of this drug every eight hours for the relief of pain. For the next twelve days the patient was able to obtain relief with two injections daily, each dose being 100 mg.

From August 16 until the present time (September 16) the patient has received 150 mg. of tetraethylammonium chloride intramuscularly three times a day, with relief of pain for six to eight hours after each injection. She remarked that the pain when present is not so severe as prior to the initiation of therapy.

CASE 3.—A white woman aged 46 was first seen on April 17, 1947, at which time she complained of severe pain in the left scapular area which radiated around the left side of the chest beneath her breast to the midline anteriorly. She did not complain of any cutaneous rash along the area of pain. The past history was noncontributory.

Physical Examination.—The patient was 5 feet 1¼ inches (155.6 cm.) tall and weighed 191 pounds (86.6 Kg.). Her temperature and pulse and respiratory rates were within the limits of normal. Her blood pressure was 168 systolic and 104 diastolic. Her fundi showed grade 2 tortuosity and narrowing of the arteries. There was a large nodular mass on the left side of her neck, which rose and fell on swallowing. There was tenderness on palpation of the left side of the chest, extending from the angle of the left scapula around beneath the breast and ending in the midline anteriorly. The left border of her heart was 2 cm. beyond the mid-

clavicular line. A roentgenogram of the chest revealed prominence of the left ventricle and aorta, which was compatible with the patient's habitus. A roentgenogram of the dorsal portion of the spine revealed multiple, unfused epiphyses at the margins of the vertebral bodies. There was also osteoarthritic lipping. These findings were compatible with an old epiphysitis and osteoarthritis.

Laboratory studies revealed that the hemoglobin concentration and red cell, white cell and differential counts were within normal limits. The urine was normal; the Kahn and Kline reactions were negative, and the sedimentation rate was normal. A four lead electrocardiogram was interpreted as normal. Microscopic examination of the bone marrow did not reveal any abnormalities. A spinal puncture on April 27 did not reveal any alteration in the pressure or dynamic status; the cell count and the colloidal gold curve were normal, and the Kahn and Kline reactions were negative. The blood calcium, phosphorus, total protein, albumin-globulin ratio and alkaline and acid phosphatase were within the limits of normal. A neurologic consultation on April 22 confirmed our diagnosis of intercostal neuralgia.

As soon as the patient was seen, and while her diagnostic examination was being completed, she was given 10 grains (0.65 Gm.) of sodium salicylate every four hours, short wave therapy to the left side of her chest and ½ grain (0.03 Gm.) of codeine sulfate every four hours as necessary to relieve pain. The patient was seen daily in the outpatient department and failed to respond to therapy.

On April 22 she was given "pantopon" (a preparation containing the total opium alkaloids as soluble hydrochlorides), ⅓ grain (0.02 Gm.) every four hours as necessary for relief of pain. She was unable to obtain any relief. On April 28 she was hospitalized and given 50 mg. of tetraethylammonium chloride intramuscularly in the morning and at bedtime. After the first day of therapy she noticed complete relief of pain lasting six hours, with each injection. Two injections of tetraethylammonium chloride were given daily until May 10, at which time she was free of pain. She was then given 50 mg. of this drug every other day until May 16, when all therapy was discontinued because of cessation of symptoms.

CASE 4.—A white woman aged 74 was first seen in the outpatient department on July 30, 1947. She had felt well until six weeks before, when she began to note a "pressing pain" in the left lower part of the chest. The pain was severe enough to require sedation and anodynes. Ten days before her first visit to the clinic she noted a small patch of blisters beneath the left breast. Within forty-eight hours, the blisters had formed a band around the left side of her chest and extended to the midline posteriorly. With the onset of the vesicles, she noted a severe "jabbing pain" in the left lower part of the chest and the left scapular area. The past history was noncontributory.

Physical examination revealed an acutely ill, obese woman, who was experiencing severe pain. Her temperature, pulse and respiration were normal, and her blood pressure was 112 systolic and 64 diastolic. A band of dermatitis extended from the midline anteriorly, beneath the left breast and continued posteriorly to the angle of the left scapula and ended at the midline. This area of dermatitis was 6 cm. wide and consisted of small vesicles between scattered areas of eschar. The rest of the physical examination revealed nothing abnormal except for complete prolapse of the uterus.

A roentgenogram of the chest on July 30 showed moderate degenerative cardiovascular disease which was compatible with her age. A multiple lead electrocardiogram on the same date revealed low voltage. The Kahn and Kline reactions were negative, and the urine, hemoglobin concentration and red cell, white cell and differential counts were within normal limits.

On August 5 she was given 50 mg. of tetraethylammonium chloride with relief of pain in the chest. The following day she informed us that at 1 o'clock a. m. she was awakened by a lancinating pain in the left lower part of the chest and took ½ grain (0.03 Gm.) of codeine sulfate for relief. On August 6 she was given 100 mg. of tetraethylammonium chloride intramuscularly at bedtime. She was free of pain until 7 a. m. the following day, when she was again awakened by lancinating pain. Relief was obtained by using codeine sulfate, ½ grain (0.03 Gm.). On August 8 she was given 150 mg. of tetraethylammonium chloride and did not experience any pain throughout the night. On August 10 the pain had not returned, and it was noted that no fresh lesions had appeared. All the vesicles had been converted into an eschar.

Three days later she noted a return of pain and was unable to sleep at night. The eschar had disappeared, leaving blotchy red areas. On August 14 the patient was given 100 mg. of tetraethylammonium chloride at bedtime. She did not experience pain until 7 a. m. on August 17. On that date she was given 100 mg. of this drug, and she remarked that the pain was greatly relieved. When seen on August 26, she remarked that she had been free from pain in the chest since her last injection, and therefore therapy was discontinued.

SUMMARY AND CONCLUSIONS

Block of the autonomic ganglia has been established as the best form of therapy of herpes zoster and related painful conditions. Procaine block of the autonomic ganglia is not always feasible because of the lack of technical skill. Tetraethylammonium chloride has been administered without danger if the necessary precautions have been observed, thus making block of the autonomic ganglia available to the medical profession. Tetraethylammonium chloride permits the patient with herpes zoster to be ambulatory, and with repeated injections the pain is controlled.

Three cases of herpes zoster and 1 case of intercostal neuralgia are presented. Treatment with tetraethylammonium chloride resulted in complete relief of pain in 2 instances within a short time after therapy was initiated, whereas in the 2 cases of herpes zoster continuous injections of this drug were required over periods of one and three months, respectively. The relief of pain following block of the autonomic ganglia with tetraethylammonium chloride is dramatic and is an excellent treatment for herpes zoster and intercostal neuralgia.

987 East Jefferson Avenue.

NEUROLOGIC MANIFESTATIONS ASSOCIATED WITH VITAMIN A DEFICIENCY IN YOUNG DUCKS

A Clinical and Pathologic Study

D. E. FLETCHER, Ph.D., M.D.
AND
R. H. RIGDON, M.D.
LITTLE ROCK, ARK.

TWO OPPOSING views are held regarding the clinical manifestations of the pathologic changes in the nervous system that result from vitamin A deficiency. One group of investigators [1] observed weakness, incoordination and ataxia in their experimental animals, and they demonstrated lesions in the brain, spinal cord and peripheral nerves. A second group [2] found no significant clinical or pathologic changes in their vitamin A–deficient animals. There was a difference

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From the Department of Pathology, University of Arkansas School of Medicine.

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The vitamin A–deficient rations were supplied by the Ralston Purina Company, St. Louis. The vitamin A determinations on the livers were made by the Nutrition Research Laboratories of the Ralston Purina Company.

1. (*a*) Hughes, J. S.; Lienhardt, H. F., and Aubel, C. E.: Nerve Degeneration Resulting from Avitaminosis A, J. Nutrition **2**:183, 1929. (*b*) Irving, J. T., and Richards, M. B.: Early Lesions of Vitamin A Deficiency, J. Physiol. **94**:307, 1938. (*c*) Mellanby, E.: The Experimental Production and Prevention of Degeneration in the Spinal Cord, Brain **54**:247, 1931. (*d*) Zimmerman, H. M.: Lesions of the Nervous System in Vitamin Deficiency: I. Rats on a Diet Low in Vitamin A, J. Exper. Med. **57**:215, 1933. (*e*) Zimmerman, H. M., and Cowgill, G. R.: Lesions in the Nervous System in Vitamin Deficiency: IV. The Effect of Carotene in the Treatment of the Nervous Disorder in Rats Fed a Diet Low in Vitamin A, J. Nutrition **2**:411, 1936. (*f*) Aberle, S. B. D.: Neurological Disturbances in Rats Reared on Diets Deficient in Vitamin A, ibid. **7**:455, 1934.

2. (*a*) Eveleth, D. F., and Biester, H. D.: The Significance of Myelin Sheath Degeneration and Its Relation to Incoordination, Am. J. Path. **13**:257, 1937. (*b*) Grinker, R. R., and Kandell, E.: Experimental Vitamin (A, B_1, B_2, and B Complex) Deficiency: Histological Changes in the Central Nervous System, Arch. Neurol. & Psychiat. **30**:1287 (Dec.) 1933. (*c*) Suzman, M. M.; Muller, G. L., and Ungley, C. C.: An Attempt to Produce Spinal Cord Degeneration in Dogs Fed a High Cereal Diet Deficient in Vitamin A: Incidental Development of a Syndrome of Anemia, Skin Lesions, Anorexia and Changes in the Concentration of Blood Lipoids, Am. J. Physiol. **101**:529, 1932.

of opinion among the former group as to the mechanism of formation of the pathologic changes. Mellanby [1c] expressed the opinion that the degenerative changes in the central nervous system and peripheral nerves are specific for avitaminosis A, whereas Wolbach and Bessey [3] stated the belief that the lesions result from a mechanical distortion produced by the differential rate of growth between the spinal cord and the vertebral column.

Recently, in a study in this laboratory of malaria in ducks fed a vitamin A–deficient diet, it was observed that the birds became weak and were ataxic and that many of their movements were incoordinated.[4] This observation stimulated the study of the lesions in the nervous system of vitamin A–deficient ducks. Both the clinical manifestations and the neuropathologic changes are reported in this paper.

MATERIAL AND METHODS

One day old white Pekin ducks, obtained from a commercial hatchery, were divided into small groups and kept in a battery where food and water were available at all times. They were fed the following vitamin A–deficient ration:

	Percentage
Mineralized salt	0.25
Puriflavin (250)® *	1.00
Calcium carbonate	2.00
Wheat germ	5.00
Soybean oil meal	18.00
Fish meal (60%)	6.00
Meat scraps	4.00
Brewers' yeast	5.00
Ground wheat	19.65
White corn	29.00
Ground oats	5.00
Molasses	5.00
Dry vitamin D (2,000 U. S. P. units of vitamin D)	0.10
* The composition of puriflavin®, expressed in milligrams per hundred grams of ration is as follows:	
Thiamine hydrochloride U. S. P.	0.5
Riboflavin U. S. P.	0.5
Choline chloride	200.0
Folic acid	0.5
Nicotinic acid U. S. P.	5.0

The control birds were divided into two groups. One group was fed the vitamin A–deficient diet supplemented with vitamin A; 2,500 units of a preparation of vitamin A (alphalin,® 1 capsule, Eli Lilly & Co.) was given every other day. The second group was fed Purina Duck Startena® and Purina duck growena® standard rations, made by the Ralston Purina Mills.

The determination of vitamin A in the liver was made on ducks killed at various ages. The tissue was removed immediately, and it was kept frozen until the tests were made. The antimony trichloride test was used. Pathologic studies were made on 35 ducks. In the table are summarized the data relating to the number and age of the ducks used in each group, their ration and the vitamin A content of the

3. Wolbach, S. B., and Bessey, O. A.: (*a*) Tissue Changes in Vitamin A Deficiency, Physiol. Rev. **22**:233, 1942; (*b*) Vitamin A Deficiency and the Nervous System, Arch. Path. **32**:689 (May) 1941.

4. Rigdon, R. H.: Effect of Vitamin A Deficiency on P. Lophurae Infection in Ducks, J. Infect. Dis. **79**:272, 1946.

livers. Fourteen of the ducks were killed by decapitation and 21 by severing the carotid arteries and jugular veins. The brains, spinal cords, peripheral nerves and ganglia were carefully removed and immediately fixed in Bouin's solution and in a dilute solution of formaldehyde U. S. P. (1:4). Paraffin sections were prepared and stained with hematoxylin and eosin, thionine for Nissl substance, iron hematoxylin for myelin sheaths, ammoniacal silver hydroxide for nerve cells and their processes and Masson's trichome method for connective tissue.

CLINICAL OBSERVATIONS

Muscular weakness, incoordination, ataxia and paralysis were the characteristic neurologic manifestations observed in young ducks fed a vitamin A–deficient diet. The first neurologic disturbance was

Data on Ducks Used in Experiment

Number of Ducks in Each Group	Age in Days	Ration	Units of Vitamin A per Gram of Liver Tissue	Comments
9	11	Vitamin A deficient	0.0	Vitamin A determined for only 2 ducks
4	11	Vitamin A deficient plus vitamin A		
2	11	Standard	6.7 7.8	Control ducks
1	12	Vitamin A deficient		
2	13	Vitamin A deficient	104.0	Duck with 104 units of vitamin A received 1 capsule of alphalin ® 24 hours before death
1	14	Vitamin A deficient		
7	15	Vitamin A deficient	0.0 4.63	Vitamin A determined for only 2 ducks
1	15	Vitamin A deficient plus vitamin A	178.8	Control duck
2	16	Vitamin A deficient	0.0 4.4	
1	16	Vitamin A deficient plus vitamin A	167.2	Control duck
2	17	Vitamin A deficient		
2	18	Vitamin A deficient		
1	24	Vitamin A deficient	0.0	

manifested as generalized muscular weakness and appeared about the seventh or eighth day. This was more evident in the muscles of the neck, as shown by the inability of the birds to stabilize their head movements. These symptoms progressively increased in severity until incoordination and ataxia were definitely established, on the tenth to the fifteenth day. At this time the ducks stood in a semisquatting position with their feet spread widely apart. They rocked backward and forward, and their heads were continuously moving in a haphazard and purposeless quasicircular manner. When forced to walk, these ducks fell forward, backward or sidewise. Moribund birds showed neuromuscular collapse. They lay motionless on their sides. When supported on their feet they showed muscular rigidity and spasticity. They assumed a position of hyperextension and frequently fell over onto their backs. Complete paralysis occurred before death.

PATHOLOGIC OBSERVATIONS

The brains and spinal cords were exposed by removing the cranial vault and the spines and laminas of the vertebrae. The portion of the brain lying cephalad to the tentorium cerebelli showed no gross changes. There was no apparent discrepancy between the volume of the brain and the size of the cranial cavity. Numerous tumor-like masses protruded from the surface of the spinal cord (fig. 1). These were more numerous along the cervical and lumbar enlargements and along the dorsal and lateral surfaces of the cord. The intervening portion of the cord was either normal in size or greatly constricted. The spinal cord in certain

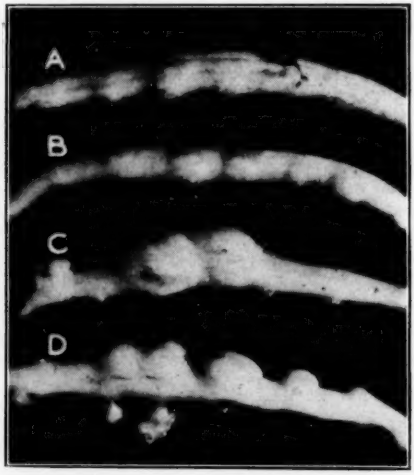

Fig. 1.—Ducks maintained for ten to fifteen days on a vitamin A–deficient diet showed multiple tumor-like masses protruding from the surface of the spinal cord. These were more numerous in the cervical and lumbar enlargements and occurred predominantly along the dorsal and lateral surfaces. They were produced by buckling, twisting and telescoping of the spinal cord. The specimens shown in this figure were taken from the lower cervical segments. (*A* and *B*) The first indications of these tumor-like swellings appeared about the seventh day, before any definite clinical disturbances were manifested. (*C* and *D*) Advanced lesions, consisting in striking alteration of the cord, were accompanied with motor weakness, incoordination, ataxia and paralysis.

places appeared several times its normal size. The vertebral canal was enlarged in such areas to accommodate the increased size of the cord. The spinal ganglia were located partly within and partly external to the intervertebral foramens. The dura mater and the arachnoid were not involved in these tumor-like masses. In no instance were any bony spicules observed to extend from the vertebrae through the dura into the substance of the cord. Gross hemorrhages occurred within the

spinal cord; these were confined to the medullary substance and were more numerous in the upper cervical segments and in the spinal medulla.

Microscopic sections through these swellings in the spinal cord revealed that in certain cases the normal relation between the gray and the white matter was not significantly disturbed. However, the size of the cord was greatly enlarged, owing to the increasing volume of the

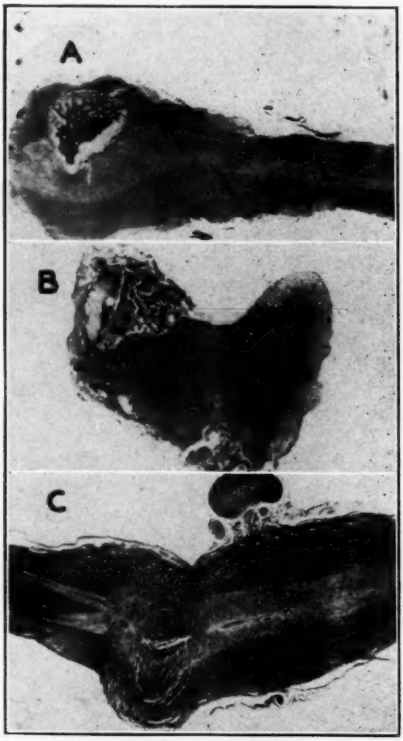

Fig. 2.—Sections through the tumor-like masses showing pronounced distortion and destruction of the neural tube. *A*, longitudinal section of the spinal cord, showing bone formation within the gray substance. The cord is notably increased in size. *B*, longitudinal section through a nodular area, showing formation of cartilage and bone, with extensive destruction of the cord substance; hematoxylin and eosin; × 10. Osteoblasts, osteoclasts and hemopoietic cells are present in such areas of bone formation. *C*, longitudinal section, showing buckling of both the gray and the white substance; myelin sheath stain; × 10. Note the swelling on one surface and the indentation on the opposite one.

gray and the white substance. These sections appeared like normal sections from a very large cord. In other cases there occurred simple mechanical buckling of the entire cord, which produced a bulge on one surface and a depression on the opposite surface (fig. 2 *C*).

Other nodules consisted primarily of either gray substance or white matter. This suggested a slipping or a telescoping of the gray and white columns over each other (fig. 3 *A*). Occasionaly the distortion was so pronounced that a cross section of the gray column appeared in a longitudinal section of the cord (fig. 3 *B*). Hyaline cartilage and bone formation were observed in many of these nodular swellings. In some cases this occurred in the white matter adjacent to a thickened pial-glial membrane (fig. 2 *B*), whereas in other cases it was located deep within the gray substance (fig. 2 *A*). Osteoblasts and osteoclasts were seen in most of these areas, and occasionally bone marrow cells were present. In many places a transition into cartilage and bone from what was thought to be connective tissue was seen. In a few instances

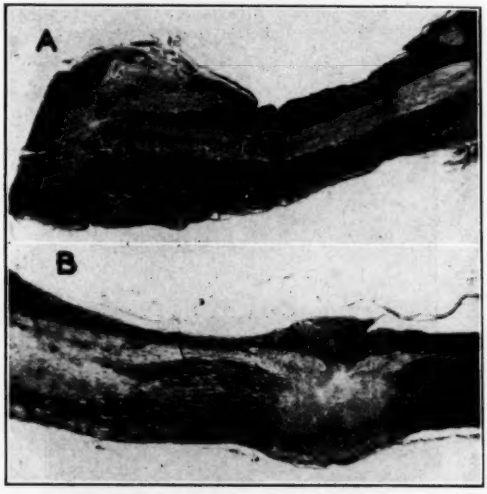

Fig. 3.—Buckling, twisting and sliding of the gray and white columns over each other characterized many of these lesions. *A*, longitudinal section of the spinal cord, showing the gray column telescoped into the white column. The gray substance extends to the surface of the cord. *B*, distortion of the cord, which may be so extensive that a cross section of the gray column appears in a longitudinal section. Note the nerve cells in the ventral gray horns of the cross section. Myelin sheath stain; × 10.

bone formation also occurred in the cerebral hemispheres along the pial-glial membrane, but this was not a conspicuous feature. Marked destruction of the gray substance occurred in the areas of hemorrhage (fig. 4 *B* and *C*). Acute necrosis was noted frequently in regions of hemorrhage (fig. 5). This necrotic tissue appeared in hematoxylin and eosin-stained sections as masses of homogeneous, pink-staining material separated by strands of fibers and blood vessels. The proliferation of blood vessels, connective tissue and glial fibers filled in

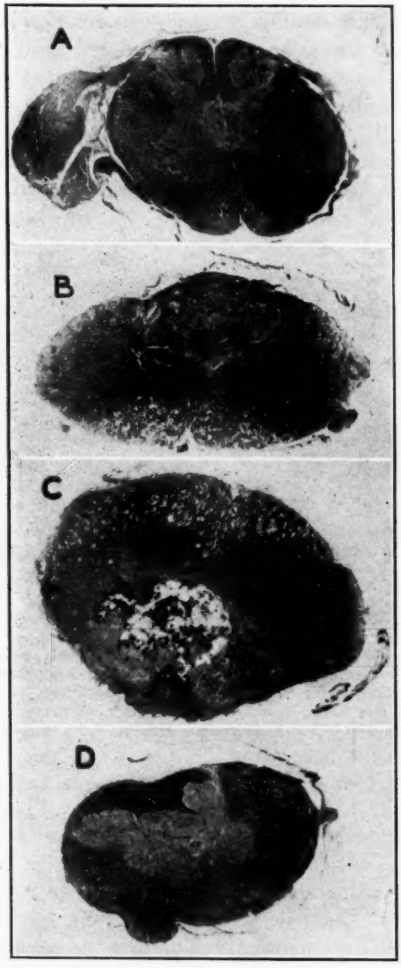

Fig. 4.—Marked swelling of the cord and hemorrhage and necrosis occurred in many sections. These were more numerous in the upper cervical region and in the spinal medulla. *A*, section through the lower cervical region of the normal spinal cord of the duck. This may be compared with the abnormal sections for size, shape and relations. *B*, massive hemorrhage into the central region of the lower cervical portion of the cord. The gray matter is practically destroyed. The white columns show extensive degeneration. *C*, hemorrhage with destruction and cavity formation. The cord is greatly increased in size. *D*, tumor-like nodules on the lateral and ventral surfaces. The dorsal gray horn extends into the lateral swelling. Marked distortion of both the gray and the white substance is clearly evident. Myelin sheath stain; × 10.

older areas of hemorrhage and necrosis. Practically every section of the spinal cord and medulla showed degeneration of the myelinated fiber tracts. This was pronounced in scattered areas (fig. 4 *B* and *C*). The spinal ganglia and peripheral nerves showed degeneration of both nerve cells and fibers. These changes were only minor, however, as compared with the extensive damage present in the spinal cord. Except for an occasional small area of bone formation, no significant histologic changes were present in the cerebellum or the cerebrum.

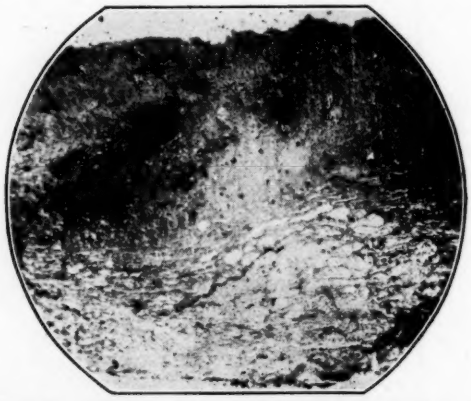

Fig. 5.—Hemorrhage and necrosis characterized many sections of the medulla. The necrosis occurs primarily in the ventral region and appears in sections stained with hematoxylin and eosin as masses of homogeneous, pink-staining material separated by fibers and blood vessels. Degeneration of nerve cells and fiber tracts accompany the hemorrhage and necrosis. Hematoxylin and eosin stain; × 100.

COMMENT

Young Pekin ducks maintained for a period of ten to fifteen days on a vitamin A–deficient diet manifested muscular weakness, incoordination, ataxia and paralysis. Degenerative changes occurred in both the central and the peripheral nervous system of these birds. The pathologic changes were more pronounced in the medulla and the spinal cord. These consisted of folding, buckling and twisting of the neural tube; sliding of the gray and white columns over each other; hemorrhage and necrosis of both the gray and the white substance; intramedullary cartilage and bone formation, and degeneration of the nerve cells and fiber tracts.

Several investigators have described degenerative changes in the nervous system of animals with vitamin A deficiency. There is, however, a considerable difference of opinion regarding the etiology and pathogenesis of these lesions. Melanby [1c] observed motor weakness, incoor-

dination and spasticity in dogs, rats and rabbits kept on a vitamin A–deficient diet, and in these animals he described degeneration of the myelinated fiber tracts of the spinal cord and of the peripheral nerves. He asserted that these changes were specific for avitaminosis A. Zimmerman [1d] (1933) found similar clinical and pathologic changes in rats maintained on a diet deficient in vitamin A. He stressed the degenerative lesions in the peripheral nerves and stated that the changes in the spinal cord were secondary to the lesions of the peripheral nerves. Wolbach and Bessey [3] (1941 and 1942) observed that if very young rats were made deficient in vitamin A degenerative lesions developed in the nervous system, whereas this did not occur when older animals were used. This significant observation may explain the negative findings of Suzman, Muller and Ungley [2c] (1932) and of Grinker and Kandell [2b] (1933). Wolbach and Bessey stated the belief that when vitamin A deficiency was established at an early age there occurred a retardation of skeletal growth, whereas the nervous system continued its normal rate of development. This produced a distortion of the nervous system in the vertebral canal and cranial cavity. They maintained therefore that the lesions which occurred in the nervous system were the result of the mechanical distortion produced by the differential rate of growth between the spinal cord and the vertebral column. They expressed the belief that vitamin A deficiency per se had no significant effect on the nervous system. They supported their contention with the observation that when very young animals were fed vitamin A–deficient rations the disproportionate rate of growth between the central nervous system and the bony column led to multiple herniations of the brain substance into the venous dural sinuses and to an overcrowding of the spinal cord, with herniation of the nerve roots into the intervertebral foramens and into the bodies of the vertebrae.

Our observations on the duck tend to support the observations and interpretations of Wolbach and Bessey.[3a] The extreme buckling and twisting of the spinal cord suggests overcrowding and indicates that the cord may have been growing at a rate far in excess of that of the vertebral column. According to Wolbach and Bessey's interpretation, one might expect a more pronounced change in the duck, in view of the fact that this bird is perhaps one of the most rapidly growing of all laboratory animals.

Certain features of our experimental findings, however, cannot be explained satisfactorily on a purely mechanical basis. The constant location of the tumor-like masses along the dorsal and lateral surfaces of the cord and their concentration in the cervical and lumbar enlargements are difficult to understand on a mechanical basis. If this is simply a matter of overgrowth, why should the cord buckle dorsolaterally much oftener than ventrolaterally? Furthermore, why should the

upper cervical and thoracic regions of the cord be comparatively exempt from distortion? This suggests that there must be differential rates of growth within the various regions of the spinal cord which determine how and where the cord will fold or bulge. The answer to these questions presupposes a knowledge of the differential rate of growth of the spinal cord of the duck and the effect, if any, of vitamin A deficiency on such growth differentials. This information is not at present available.

The apparent sliding of the gray and white columns over each other is a second feature difficult to explain on a purely mechanical basis. This also would suggest a differential growth factor. The more frequent occurrence of massive hemorrhage and necrosis in the spinal medulla and the upper cervical portion of the spinal cord, where the distortion is comparatively mild, is a third interesting feature. If the hemorrhage and necrosis are the result of the occlusion of the blood supply produced by the bending and twisting of the cord, why would not these lesions occur oftener in the regions of the cord where bending and twisting occur more frequently? The variation in the blood supply to the different regions of the cord cannot fully explain this finding. With regard to this feature, it is interesting to note that Irving and Richards [1b] (1938) emphasized the degenerative changes in the lower part of the medulla in their rats maintained on a low vitamin A diet.

The absence of any significant changes in the cerebrum of the ducks suggests two things: First, the brain may have failed to grow at a faster rate than the cranial cavity; and second, the tentorium cerebelli may have served as a check which prevented the increased intraspinal pressure from being transmitted to the cranial cavity. With regard to the first possibility, either the brain failed to grow at a normal rate, or the cranial bones did not cease growing. Both alternatives are contrary to accepted facts. Although the vitamin A–deficient ducks were smaller than the normal controls of the same age, the brains were not significantly smaller. This suggests that the brains must have developed at an approximately normal rate. If this is true, then the cranial bones also had to grow at a normal rate, which fact is contrary to the observation that the skeletal system is retarded, or even ceases growing, in vitamin A deficiency states.[5] Why this apparent discrepancy? Furthermore, if it is purely mechanical force within the vertebral canal

5. (*a*) Hess, A. F., and Pappenheimer, A. M.: Experimental Rickets in Rats: The Failure of Rats to Develop Rickets on a Diet Deficient in Vitamin A, J. Biol. Chem. **47**:395, 1921. (*b*) Tozer, F. M.: The Effect on the Guinea Pig of Deprivation of Vitamin A and of the Antiscorbutic Factors with Special Reference to the Conditions of the Costochondral Junctions of the Ribs, J. Path. & Bact. **24**:306, 1921. (*c*) Wolbach, S. B., and Howe, P. R.: Tissue Changes Following Deprivation of Fat Soluble A Vitamin, J. Exper. Med. **42**:753, 1925.

that is limited cephalad by the tentorium cerebelli, why should the cerebellum, which is subtentorial in position, be free from either gross or microscopic changes?

Finally, the formation of cartilage and bone within the medullary substance of the neural tube does not lend itself to a mechanical explanation. This is histologically true cartilage and bone, and not merely a deposition of calcium salts in scar tissue. Careful examination of the brains and spinal cords from a large series of both normal and pathologic ducks killed in this laboratory during the course of experimental studies on malaria, anoxia and hypoglycemia failed to show any evidence of cartilage or bone formation. This suggests that vitamin A deficiency per se may produce a disturbance in the metabolism of the nervous system of ducks. This may represent a metaplasia of connective tissue into cartilage and bone, similar to the well established process of epithelial metaplasia in vitamin A deficiency.[5c] If this is the case, why should the process be confined to the central nervous system? On the other hand, it may be an expression of the "overgrowth" phenomenon of bone formation described by Melanby.[6]

It is evident from our study that the problem of the effect of vitamin A deficiency on the nervous system is not entirely settled. The mechanical factor postulated by Wolbach and Bessey undoubtedly plays a prominent part in the pathogenesis of the lesions; however, there are other seemingly important factors which cannot be disregarded. Further studies, particularly along the lines of growth differentials, are indicated.

SUMMARY

Young Pekin ducks maintained for a period of ten to fifteen days on vitamin A-deficient rations manifested muscular weakness, incoordination, ataxia and paralysis. The significant pathologic changes in the central nervous system were buckling and twisting of the spinal cord, sliding of the gray and white columns over each other, hemorrhage and necrosis of the gray and white matter, degeneration of the fiber tracts and nerve cells and intramedullary formation of cartilage and bone. Although the chief etiologic factor responsible for these lesions may be the disproportionate rate of growth between the neural tube and the vertebral column, it is suggested that there is also an alteration in the differential rates of growth of various regions of the spinal cord. It is believed that vitamin A deficiency may affect adversely these growth potentials.

University of Arkansas School of Medicine (Dr. Fletcher).
University of Texas School of Medicine, Galveston, Texas (Dr. Rigdon).

6. Mellanby, E.: Skeletal Changes Affecting the Nervous System Produced in Young Dogs by Diets Deficient in Vitamin A, J. Physiol. **99**:467, 1941.

News and Comment

THE AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY, INC.

The following specialists were certified at a meeting of the Board in New York, in December 1948:

Psychiatry.—Eduard Ascher, Baltimore; Charles Beck, New York; Eric Bell Jr.; Cleveland; Herman S. Belmont, Philadelphia; Ralph D. Bergen, Chicago; Irving L. Berger, Cleveland; Isidor Bernstein, New York; Ivan F. Bird, Trenton, N. J.; Estelle P. Boynton, Atlanta, Ga.; Claude H. Butler, Norristown, Pa.; *J. Robert Campbell, Tampa, Fla.; Dante V. Capra, Dorchester, Mass.; William G. Carman, Pittsburgh; Joseph O. Chassell, Stockbridge, Mass.; Irving Chelnek, Tomah, Wis.; William A. Console, New York; William R. Corcoran, Coatesville, Pa.; *Robert L. Craig, Durham, N. C.; Wesley Y. Culver, Astoria, N. Y.; Daniel Davis, Dallas, Texas; James G. Delano, Philadelphia; Edward Dengrove, Interlaken, N. J.; Murray A. Diamond, New York; Richard d'Isernia, Flushing, N. Y.; John F. Donohue, Chicago; Raymond B. Dryer, Poynette, Wis.; Robert H. Dunn, Tugus, Maine; Ada B. Dunner, Des Moines, Iowa; F. A. Dunsworth, Halifax, Nova Scotia, Canada; Ruth Ehrenberg, Boston; Lloyd C. Elledge, Danville, Ill.; Elizabeth S. Ells, Perry Point, Md.; Walter H. Faust, North Little Rock, Ark.; Philip Feinberg, Perry Point, Md.; Andrew Fergus, Canandaigua, N. Y.; William F. Finzer, Courthouse, Reading, Pa.; Martin A. Fischer, Toronto, Canada; Gerard Fountain, Scarsdale, N. Y.; John J. Francis, Catonsville, Md.; Alma Freeman, Poughkeepsie, N. Y.; Joseph W. Friedlander, Chicago; Francis A. Gagliardi, Jamaica, N. Y.; Miles D. Garber, Norristown, Pa.; Joseph J. Geller, Paterson, N. J.; Jules Gelperin, Highland Park, Ill.; Elias H. Gerchick, New York; Jacob B. Gier, Topeka, Kan.; Morris I. Goldin, Eloise, Mich.; Abe A. Goldman, Ann Arbor, Mich.; Jewett Goldsmith, Durham, N. C.; Arthur Gorfinkel, Wingdale, N. Y.; Charles Greenberg, Wingdale, N. Y.; Alphonso Guiglia, Louisville, Ky.; Louis Halperin, Little Rock, Ark.; Steven Hammerman, Philadelphia; Van B. Osler Hammett, Philadelphia; Alfred A. Hellams, Chicago; Lore Hirsch, New York; Maria K. Hoefer, New York; William G. Hollister, Fort Worth, Texas; Harry S. Howard, Kalamazoo, Mich.; Laura K. Howard, Hartford, Conn.; A. Chapman Isham, Bronxville, N. Y.; Don E. Johnson, Philadelphia; Milton E. Jucovy, New York; John L. Kelly, Greystone Park, N. J.; Adele C. Kempker, St. Louis; Edward Kezur, Hamilton, Ohio; Frank Kiesler Jr., Minneapolis; John C. Kindred, Astoria, N. Y.; Bernard E. Kline, Chattahoochee, Fla.; Peter H. Knapp, Boston; Benjamin Kovitz, Columbus, Ohio; William C. Lewis, Topeka, Kan.; Jack London, Brooklyn; Vivion F. Lowell, Ypsilanti, Mich.; Milton Lozoff, Topeka, Kan.; Leo Madow, Philadelphia; Edward H. Malone, Boston; Robert H. McCarter, Boston; Thomas M. McMillan, Galveston, Texas; Jacob Mesken, Bridgeport, Conn.; Joseph Michaels, Bronx, N. Y.; Henry H. W. Miles, Boston; Holland C. Mitchell, Waco, Texas; John F. Oliven, New York; Lewis C. Overholt Jr., Denver; Joseph B. Parker Jr., Durham, N. C.; Hugo B. Paul, Washington, D. C.; Beatrice Postle, Athens, Ohio; Ralph D. Rabinovitch, New York; Eugene Revitch, Lyons, N. J.; George Rosenberg, Murfreesboro, Tenn.; Marion E. Roudebush, Hyattsville, Md.; Herman D. Rudnick, Philadelphia; Martin Rudoy, Brooklyn; Irving Sarnoff, New York; Simone J. Scarano, Astoria, N. Y.; Otto Schaefer, Butler, Pa.; Gabriel Schein, West

Brentwood, N. Y.; Piroska Selymes, Cleveland; Bernard H. Shulman, Willard, N. Y.; Daniel Silverman, Philadelphia; Raymond Sobel, White Plains, N. Y.; Adolph Soucek, Madison, Wis.; Jay Stanton, Great Neck, N. Y.; Philip P. Steckler, Syracuse, N. Y.; James A. Stringham, Canandaigua, N. Y.; Leonard Taboroff, Topeka, Kan.; Zelda Teplitz, Chicago; Joe E. Tyler, North Little Rock, Ark.; William V. Walsh, North Little Rock, Ark.; Charles R. Walton, Montgomery, Ala.; Louis Weinstein, Marion, Ind.; Cecil L. Wittson, Central Islip, N. Y.; Frederic G. Worden, Baltimore; George P. Wyman, Marion, Ind.; Leon Yochelson, Washington, D. C.

Neurology.—Winslow J. Borkowski, Philadelphia; Robert Cohn, Bethesda, Md.; Joseph M. Foley, Boston; Alvin I. Goldfarb, Newtown, Conn.; Max Goldman, Boston; Hubert S. Howe, New York; George L. Maltby, Portland, Maine; Murray E. Margulies, Brooklyn; Jerome K. Merlis, Framingham, Mass.; Ludlow M. Pence, Dallas, Texas; Roy L. Swank, Montreal, Canada; Frederick E. G. Valergakis, New York; *Edward K. Wilk, Middletown, Conn.; *Mark Zeifert, North Little Rock, Ark.

Neurology and Psychiatry.—Ernst Haase, Chicago.

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*The asterisk denotes complementary certification.

THE NATIONAL COMMITTEE ON ALCOHOL HYGIENE, INC.

The scientific committee of the National Committee on Alcohol Hygiene, Inc., reports that activity projects for the ensuing year are to be directed along the following lines:

1. Acquaintance of teen-agers and senior high school and young college students with the medical-psychologic facts about alcohol, alcoholic beverages and the alcoholic addict.

2. Integration of a director-training program, through cooperation with the United States Public Health Service, Division of Mental Hygiene; the School of Hygiene of the Johns Hopkins Hospital, and medical physicians interested in alcoholism from the medical point of view. Such a program would benefit community clinics, such as the Alcohol Clinic of the District of Columbia, and other centers which need or wish to head the staff with a director who is competent and experienced in this field.

3. Presentation to the general hospital of medical facts about treatment of acute alcoholism and alcoholism in general, and the gaining of their cooperation in providing medical aid.

At the annual meeting, in October, the following officers were elected: president, Robert V. Seliger, M.D., chief psychiatrist, Neuropsychiatric Institute of Baltimore; vice president, Lawrence F. Woolley, M.D., psychiatrist, Emory University Hospital and Medical School, Atlanta, Ga.; secretary-treasurer, Victoria Cranford, psychotherapist, Neuropsychiatric Institute of Baltimore; assistant secretary-treasurer, Caroline Diggs, chief social worker, United States Marine Hospital, Baltimore.

In addition, the following trustees of the organization continue in office: Philip Harriman, professor of psychology, Bucknell University, Lewisburg, Pa.; John C. Krantz Jr., professor of pharmacology, University of Maryland School of Medicine, Baltimore; William Lovitt, attorney at law, Baltimore; Wendell Muncie, consulting psychiatrist, Baltimore; Horace K. Richardson, consulting psychiatrist, Baltimore; G. Wilson Shaffer, Dean of the Undergraduate Schools of Johns Hopkins University, Baltimore.

The scientific committee selected and named at the annual meeting to function with the aforenoted trustees are: Dr. Edward B. Allen, senior resident psychiatrist, New York Hospital—Westchester Division, White Plains, N. Y.; Dr. Vernon C. Branham, Veterans Administration, Washington, D. C.; Dr. Hervey M. Cleckley, professor of psychiatry, University of Georgia School of Medicine, Augusta, Ga.; Dr. G. Kirby Collier, consulting psychiatrist, Rochester, N. Y.; Dr. Robert H. Felix, Chief, Mental Hygiene Division, United States Public Health Service, Bethesda, Md.; Dr. Arthur N. Foxe, consulting psychiatrist, New York; Dr. Maurice D. Friedman, consulting psychiatrist, Cleveland; Mrs. Florence Halpern, psychologist and Rorschach expert, Bellevue Hospital, New York; Dr. Donald M. Hamilton, psychiatrist, New York Hospital—Westchester Division, White Plains, N. Y.; Dr. Harry R. Lipton, consulting psychiatrist, Atlanta, Ga.; Dr. Frank H. Luton, professor of psychiatry, Vanderbilt University School of Medicine, Nashville, Tenn.; Dr. Merrill Moore, associate in psychiatry, Harvard Medical School, Boston; Dr. Meyer Nimkoff, professor of psychology, Bucknell University, Lewisburg, Pa.; Dr. Curtis F. Prout, physician in charge of men's department, New York Hospital-Westchester Division, White Plains, N. Y.; Dr. John D. Reichard, senior surgeon, United States Public Health Service, Staten Island, N. Y.; Dr. Vernon Scheidt, psychologist, Williams & Wilkins Company, Baltimore; Dr. Lowell S. Selling, consulting psychiatrist, Orlando, Fla.; Dr. R. Burke Suitt, psychiatrist, Duke University, Durham, N. C.; Dr. David C. Wilson, professor of neurology and psychiatry, University of Virginia Department of Medicine, Charlottesville, Va.; Dr. Gregory Zilboorg, consulting psychiatrist and psychologist, New York.

TRAINING PROGRAM IN CHILD PSYCHIATRY AT THE NEW YORK UNIVERSITY–BELLEVUE MEDICAL CENTER

The department of psychiatry of the New York University–Bellevue Medical Center announces the establishment of a program for training in child psychiatry. For this purpose, there have been designated two full time residencies in child psychiatry. In July 1949 there will also be available several full time fellowships. The facilities for training include work in the children's wards and the outpatient department of the Psychiatric Division of Bellevue Hospital; in the liaison service with the department of pediatrics, and in the psychiatric division of the University Hospital.

DR. STANLEY COBB TO DELIVER SALMON MEMORIAL LECTURE FOR 1949

Dr. C. Charles Burlingame, chairman of the Salmon Memorial Committee, has announced the selection of Dr. Stanley Cobb as the Salmon Memorial Lecturer for 1949. Dr. Cobb, president of the American Neurological Association, is one of the most renowned researchers, writers and educators in the field of medicine. He has been Bullard professor of neuropathology at Harvard Medical School since 1926 and psychiatrist in chief to the Massachusetts General Hospital for the last fifteen years.

The Salmon Memorial Committee, appointed by the New York Academy of Medicine, selects each year a specialist in the fields of psychiatry, neurology or allied fields, either in this country or abroad, who has made an outstanding contribution to his specialty. Begun in 1932, the lectures have had an imposing array of specialists, including Dr. Adolf Meyer, Dr. C. Macfie Campbell, Dr. William White, Dr. Samuel T. Orton, Dr. William Healy, Dr. David Henderson, Dr. Edward Strecker, Dr. Nolan D. C. Lewis, Dr. Robert Dick Gillespie,

Dr. Emilio Mira, Dr. Abraham Arden Brill, Dr. John Rawlings Rees, Dr. Roy Graham Hoskins, Dr. David M. Levy, Dr. Harold Dwight Laswell and Dr. Torbjoern O. Caspersson.

Dr. Cobb is the author of textbooks which have become recognized as the standard in medical schools throughout the world. Included are such works as "Borderlands of Psychiatry," "Foundations of Psychiatry," "An Outline of Neuropathology," "Preface to Nervous Disease," and "Epilepsy." He is an editor of the *American Journal of Psychiatry*, ARCHIVES OF NEUROLOGY AND PSYCHIATRY and *Medicine*.

POSTGRADUATE CENTER FOR PSYCHOTHERAPY, INC.

The Postgraduate Center for Psychotherapy, Inc., the training associate of the Institute for Research in Psychotherapy, Inc., has been granted a provisional charter from the Board of Regents of the New York State Educational Department. It offers intensive training for psychiatrists in psychotherapy leading to certification, as well as individual courses for general practitioners and nonpsychiatric medical specialists in psychotherapy and psychosomatic medicine.

Clinical psychologists and psychiatric case workers are trained in methods that are within the scope of their education and skills, and which can contribute to an integrated program.

The primary aim of the program is to encourage the development of teams of psychiatrists, psychologists and social workers who can organize and operate community psychiatric clinics.

The courses of instruction include practical demonstrations in psychotherapy, as well as lectures. The work of all students is supervised by teachers qualified to manage a specific type of problem. Before the psychiatric student completes his training, he has had personal experience under supervision in the management of various types of cases.

There are required and optional lecture courses. Courses include the principles and practice of psychotherapy; psychodynamics and psychopathology; short term psychotherapy, utilizing psychobiologic and psychoanalytic approaches; hypnotherapy; narcosynthesis; shock therapy; group therapy; case work therapy; psychologic counseling; child and adolescent psychotherapy; case conferences and seminars; organization and operation of a community psychiatric clinic; projective technics in psychotherapy; seminar on psychosomatic medicine; therapy of the neuroses and psychoses; compensation and medicolegal problems in psychiatry; anthropologic and sociologic aspects of psychiatry, and industrial psychiatry.

Therapeutic Program.—The Institute, in close cooperation with the Postgraduate Center, also will carry out a therapeutic program. This contemplated activity will consist of the extension of clinic services for those who are in need of psychiatric treatment and are unable to afford the fees of private psychiatrists.

Research.—A research program is in process to study and to evaluate all existing types of psychotherapy in order to determine their values and limitations, the kinds of patients benefited and the extent and quality of the successes achieved. The aim is to shorten treatment methods and to render them more efficient.

Public Educational Program.—The educational program is conducted along several channels: for the lay public, the general practitioner, the specialist in other branches of medicine and the psychiatrist. It is coordinated with the activities of existing agencies which are working in the same field.

Further information on this program may be obtained by writing to Stephen P. Jewett, M.D., dean, or to Miss Janice Hatcher, registrar, Postgraduate Center for Psychotherapy, Inc., 218 East Seventieth Street, New York 21.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Physiology and Biochemistry

WATER INTOXICATION AND THE ELECTROENCEPHALOGRAM. ERNST GELLHORN and H. M. BALLIN, Am. J. Physiol. **146**:559 (July) 1946.

Gellhorn and Ballin studied the electroencephalograms of rats in which water intoxication had been induced by the intraperitoneal injection of water. Slow waves of high voltage appeared and increased with water intoxication. Convulsive potentials, similar to those seen in epilepsy, occurred either as larval discharges or with convulsions. In general, the slow waves preceded the convulsive phenomena. Treatment with desoxycorticosterone acetate tended to prevent the appearance of convulsive discharges. Since petit mal, grand mal and psychomotor types of electrical changes were induced by water intoxication, Gellhorn and Ballin conclude that these types of electrical change may be due to the same basic disturbance.

FORSTER, Philadelphia.

A STUDY OF THE RESPIRATORY QUOTIENT IN EXPERIMENTAL HYPOTHALAMIC OBESITY. CHANDLER M. BROOKS, Am. J. Physiol. **147**:727 (Dec.) 1946.

Brooks found normal basal respiratory quotients for rats with obesity as the result of hypothalamic lesions. During the dynamic phase of developing obesity, the respiratory quotient was increased, but during the static phase it fell to normal. Starvation of the obese animals produced a second dynamic phase, with an increase in the respiratory quotient, but never to the extent of the initial increase.

FORSTER, Philadelphia.

A STUDY OF THE EFFECT OF HYPOTHALAMIC LESIONS ON THE EATING HABITS OF THE ALBINO RAT. CHANDLER M. BROOKS, RICHARD A. LOCKWOOD and MILTON L. WIGGINS, Am. J. Physiol. **147**:735 (Dec.) 1946.

The authors studied the time of eating and intake per feeding of rats before and after induction of hypothalamic lesions. Rats which became obese showed an increase in average meal size and also tended to eat more food during the day, rather than at night. As the static phase of obesity developed, the intensity of the hyperphagia waned. Decreasing size of the stomach did not prevent the development of obesity, for the animals ate oftener than normally. Vagotomy gave inconclusive results as to the effect on appetite and development of obesity.

FORSTER, Philadelphia.

THE CONTRIBUTORY ROLE OF THE AFFERENT NERVOUS FACTOR IN EXPERIMENTAL SHOCK: SUBLETHAL HEMORRHAGE AND SCIATIC NERVE STIMULATION. R. R. OVERMAN and S. C. WANG, Am. J. Physiol. **148**:289 (Feb.) 1947.

Overman and Wang found that electrical stimulation of the sciatic nerves in dogs subjected to sublethal hemorrhage produce a pressor effect. The clinical manifestations of dogs subjected to such hemorrhage and afferent stimulation tended to approximate those seen in traumatized animals, namely, early tachycardia, a relatively high mean blood pressure and early depression of the central nervous system. Serum protein concentrations and hematocrit values were less than the corresponding changes in the animals with simple hemorrhage.

FORSTER, Philadelphia.

EFFECT OF ORGAN EXTRACTS AND THEIR FRACTIONS ON ACETYLCHOLINE SYNTHESIS. CLARA TORDA and HAROLD G. WOLFF, Am. J. Physiol. **148**:417 (Feb.) 1947.

Torda and Wolff studied the effects of tissue extracts and various fractions of these extracts on acetylcholine synthesis. Blood serum and animal tissues contain substances that both increase and decrease acetylcholine synthesis. Human blood serum and water extracts of various animal tissues contain substances that increase acetylcholine synthesis; these substances are in part nondialyzable and in part dialyzable. Ether extracts of serum and various tissues contain factors that decrease acetylcholine synthesis, and for some of the depressor effects fatty acids are responsible.

FORSTER, Philadelphia.

AUDIOGENIC FITS PRODUCED BY MAGNESIUM DEFICIENCY IN TAME DOMESTIC NORWAY RATS AND IN WILD NORWAY AND ALEXANDRINE RATS. WILLIAM J. GRIFFITHS JR., Am. J. Physiol. **149**:135 (April) 1947.

Griffiths found that domestic, and wild Norway and wild Alexandrine rats exhibited audiogenic seizures when fed a magnesium-deficient diet, but did not have seizures in response to sound when fed normal diets. Domestic Norway rats had audiogenic seizures within a shorter period on the magnesium-deficient diet than did the other strains. The seizures were fatal to the domestic Norway rats.

FORSTER, Philadelphia.

EFFECT OF EXPERIMENTAL INSOMNIA ON THE RATE OF POTENTIAL CHANGES IN THE BRAIN. DAVID B. TYLER, JOSEPH GOODMAN and THEODORE ROTHMAN, Am. J. Physiol. **149**:185 (April) 1947.

Tyler, Goodman and Rothman studied the electroencephalograms of 12 subjects in whom they induced experimental insomnia. The electroencephalograms were analyzed by the method of Brazier and Finesinger. The authors found that changes in the state of attention or alertness, such as that produced by mental arithmetic, caused an increase in the electrical activity of the brain, the degree of increase paralleling the intensity of the mental effort. Increasing periods of insomnia also increased the electrical activity of the brain. Combining insomnia and additional mental alertness resulted in irregular changes, indicating a reduced capacity of the fatigued brain to increase further its electrical activity.

FORSTER, Philadelphia.

EFFECT OF FRONTAL LOBECTOMY ON BLOOD SUGARS OF NORMAL CATS AND MONKEYS AND ADRENAL DENERVATED CATS. MARGARET A. KENNARD, C. W. HAMPEL and M. DORRITT WILLNER, Am. J. Physiol. **149**:246 (April) 1947.

Kennard, Hampel and Willner performed bilateral frontal lobectomies on cats and monkeys. Sham rage was produced in cats but not in monkeys. In the cats there occurred increases in the blood sugar and pulse and respiratory rates. Previous denervation of the adrenal glands decrease the duration of the increase in blood sugar. The rise in blood sugar was not the result of the anesthesia or of removal of brain tissue only, for occipital lobectomies produced no alteration in the blood sugar. The changes in blood sugar, respiratory rate and pulse rate did not occur in the monkeys. The authors conclude that different autonomic patterns exist in cortical ablations in the two species, producing hyperactivity in monkeys and sham rage in cats.

FORSTER, Philadelphia.

THE LOCATION OF THE CONSCIOUS CENTER IN THE BRAIN: THE CORPUS STRIATUM. WALTER E. DANDY, Bull. Johns Hopkins Hosp. **79**:34 (July) 1946.

Material for this report was obtained from a study of 10 patients who had immediate and permanent loss of consciousness following various neurosurgical procedures. Resection of the frontal lobe was performed on 7 patients; 2 had tumors of the third ventricle, and 1 had a ligation of both anterior cerebral arteries at the internal carotid arteries. In 4 of the patients loss of consciousness persisted over fifteen, seventeen, twenty-three and fifty-one days, respectively, until death.

In all 7 cases of resection of the frontal lobe, both anterior cerebral arteries were sacrified at the genu of the corpus callosum. In only 2 of these cases were the basal ganglia carefully studied (in 1, microscopically). In 1 of these cases the brain showed direct trauma to the corpus striatum of the right side, and in the other, necrosis of the same region of the right side, due to retrograde thrombosis of the anterior cerebral artery from the genu of the corpus callosum to the internal carotid artery, including the recurrent medial striate artery (Heubner), which supplies the anterior part of the corpus striatum. Until attention was directed to the basal ganglia, it was believed that bilateral ligation of the anterior cerebral artery at the genu of the corpus callosum was adequate to explain the loss of consciousness. It is known from other bilateral ligations of the anterior cerebral artery at this point that deprivation of the blood supply of these vessels beyond the genu of the corpus callosum does not per se cause loss of consciousness.

In another case, both anterior cerebral arteries were ligated at their origin from the internal carotid arteries, and bilateral necrosis in the anterior portion of the corpus striatum resulted, a lesion which may be responsible for the loss of consciousness.

In each of the 3 carefully studied cases there was necrosis of the anterior part of the corpus striatum—in 1, of direct traumatic origin; in the other 2 from deprivation of the blood supply. In none of the 3 specimens was the thalamus involved in the necrosis (2 of these were studied microscopically).

In 2 of the 10 reported cases, the same loss of consciousness followed removal of tumors from the third ventricle without injury of either anterior cerebral artery. The results in these cases indicate that the center for consciousness is located somewhere in the basal ganglia or the thalamus, but they do not localize it precisely. It is clear that in the 7 cases of frontal lobectomy the injured part of the basal ganglia, or of its blood supply, must lie in the path of the resection, and this could be only in the anterior part of the corpus striatum. The thalamus is posterior to this line of section, and therefore not involved in the trauma.

The anterior part of the hypothalamus is also beyond the line of section of the frontal lobes and, for this reason, could not have been involved.

In 2 of the 3 cases studied, the lesion in the corpus striatum was strictly unilateral and on the right side; in the third case it was bilateral.

GUTTMAN, Philadelphia.

Psychiatry and Psychopathology

A STUDY OF THE MODIFICATION OF MENTAL ILLNESS BY INTERCURRENT PHYSICAL DISORDERS IN ONE HUNDRED PATIENTS. H. E. CLOW and C. T. PROUT, Am. J. Psychiat. **103**:179 (Sept.) 1946.

Clow and Prout studied the effects of serious medical or surgical conditions, ranging from major surgical procedures and acute infections to accidental and suicidal injuries, occurring in the course of mental illness in a group of hospitalized patients.

The mental status of 67 of the 100 patients was definitely improved; 28 continued to improve until their discharge from the hospital; 11 eventually recovered; the condition of 27 remained unchanged, and that of 6 became worse.

Improvement in the mental state was influenced by the duration of the mental illness prior to the physical disorder. Seventy-five per cent of the patients hospitalized less than one year showed improvement, whereas the condition of 40 per cent of patients hospitalized more than one year improved. Improvement was most evident in the manic-depressive group; patients with organic disease of the brain prior to physical illness did least well. Patients whose improvement was related to both electric shock therapy and intercurrent physical disorders did better in regard to the amount and the duration of improvement than did those who responded to either alone. In the group with affective disorders and passive personalities, there was a definite tendency to improvement with self-inflicted aggressive activity.

The authors hypothesize stimulation of the patient's interest toward the realistic goal of recovery through a threat to his physical existence. Aggression and interest, previously withdrawn from external reality, are directed outward. Recovery is highest in the manic-depressive depressed group because aggression is well organized in these patients, even if it is turned inward.

Two cases of complete recovery from depressed states are reported. In 1 case, recovery followed a hemolytic streptococcic infection of the throat; in the other, the patient, with suicidal intent, swallowed a dental bridge, which lodged in his bronchus.

FRANKEL, Philadelphia.

NAIL BITING: INCIDENCE, ALLIED PERSONALITY TRAITS, AND MILITARY SIGNIFICANCE. J. M. HILL, Am. J. Psychiat. **103**:185 (Sept.) 1946.

Hill studied nail biting in Naval and Marine enlisted personnel who were evacuated from the Pacific battle area to a hospital in this country because of nervous conditions. He found nail biting to be present in 100 of 223 cases representing routine admissions. In more than half this group, nail biting had been present prior to entrance into service. It tended to occur in tense emotional situations or during periods of enforced inactivity.

Seventy-three per cent of the group of nail biters had violent tempers. Those whose anger was expressed by numerous fist fights were more useful for military purposes than those who tended to weep and tremble when enraged. The latter group was more likely to become emotionally disturbed in response to combat killing.

As a control group, 100 cases of nail biting were collected in a group of 1,571 men separated under the point system. Of this group, 75 per cent had a temper of average degree; 90 per cent had experienced an average, or more than average, number of fist fights, and 93 per cent had never trembled or wept when angry.

FRANKEL, Philadelphia.

Diseases of the Brain

CEREBRAL ARTERIOSCLEROSIS WITH SMALL, COMMONLY UNRECOGNIZED APOPLEXIES. W. C. ALVAREZ, Geriatrics **1**:189 (May-June) 1946.

According to Alvarez, thromboses of small intracranial arteries are seldom recognized for what they are—exacerbations in the course of a long-lasting, eventually fatal, disease. Because of its length, the disease can usually be studied in its

entirety only in relatives or old friends. The first episodes can come in the forties, or even in the thirties. The thromboses often occur during sleep. Diagnosis is fairly easy when the patient suddenly changes in character and ability. Many have an unexplained nervous breakdown; some become psychopathic; some deteriorate morally. Occasionally one will go into a state of agitated depression. Many lose their grooming and go about with dirty clothing. Some fall unconscious. Acute episodes are often thought to be attacks of "acute indigestion." Some persons suddenly are unable to sleep. Many suffer with sudden distresses in the thorax or the abdomen. Some have indigestion as the result of spasticity of the muscle in the digestive tract. Vertigo is a common symptom. Some patients have symptoms of a slight bulbar paralysis, or manifest a parkinsonian syndrome, paresthesias or numbnesses, slight weakness of muscles, abrupt loss of considerable weight, a burning or a bad taste in the mouth, facial pain, sudden blindness or arthritis in a weakened extremity. In order to make the diagnosis, it may be necessary to talk to relatives and business associates. They will tell of the sudden aging and of extensive changes in character and ability. The physician must be careful not to let himself be led astray by inconsequential findings turned up during the examination. An important sign may be a considerable drop in blood pressure immediately after an episode. The prognosis is usually poor, but some persons work on for years. Treatment of the disease has not met with much success.

J. A. M. A.

BILATERALLY SYNCHRONOUS PAROXYSMAL SLOW ACTIVITY IN THE ELECTROENCEPHALOGRAMS OF NON-EPILEPTICS. MORTIMER OSTOW and MIRIAM OSTOW, J. Nerv. & Ment. Dis. **103**:346 (April) 1946.

The authors performed electroencephalographic studies on 440 patients and other inmates at the Medical Center for Federal Prisoners. Bisynchronous paroxysmal slow activity, evidenced by the synchronous appearance of sudden bursts of regular activity at frequencies of from 2 to 7 per second from homologous areas of the right and left sides of the head, was found to occur with an unusually high incidence.

In each of sixteen diagnostic categories, there was at least 15 per cent of this type of activity and in some nonepileptic groups it rose to 40 per cent. This incidence is in contrast to that of 0.5 to 1 per cent in the general population. The incidence for patients with confirmed epilepsy was 86 per cent, and that for persons suspected of being epileptic, 50 per cent. Patients with organic encephalopathy with convulsions showed 50 per cent of such activity, and the nonconvulsive members of this group, 25 per cent. Of 139 criminal psychopaths, there were 64 without homosexual proclivities, and of these, 27 per cent showed bisynchronous slow activity. Twenty-eight per cent of 57 criminal psychopaths who were facultatively homosexual, and 39 per cent of 18 who showed obligatory homosexuality, displayed similar electroencephalographic patterns. The activity was seen in 38 per cent of 16 mentally defective persons, in 38 per cent of 16 religious objectors to the Selective Service Act, in 18 per cent of 49 persons with simple adult maladjustment and in 13, 15, 18 and 18 per cent of schizophrenic patients classified, respectively, as having paranoid, catatonic, simple and mixed types.

Thus, regardless of diagnosis, the incidence of bisynchronous paroxysmal slow activity is many times as high among prisoners as in the general population. Such activity appears to be associated not only with epilepsy but with those personality traits which make for criminal behavior. The authors suggest that this type of

activity may be a subcortical rhythmic abnormality, probably congenital and possibly familial, which in itself is clinically silent. It is not an integral part of the convulsive seizure, but on infrequent occasions, when an individual episode succeeds in exciting the cerebral cortex, a grand or petit mal seizure may be evoked, while isolation of the cortex as a result of such an episode produces a psychomotor episode.

CHODOFF, Washington, D. C.

THE AUDITORY NERVE IN MULTIPLE SCLEROSIS. H. VON LEDEN and B. T. HORTON, Proc. Staff Meet., Mayo Clin. **22**:279 (July 9) 1947.

Von Leden and Horton report the results of their study of a series of 92 patients under the age of 50 who had no indication of previous disease of the middle ear, and who had the classic symptoms and signs of multiple sclerosis. Forty-three per cent had a measurable degree of deafness, of more than 25 decibels, in one or both ears. The decrease in hearing in the speech range usually did not extend beyond the critical level of 30 decibels; only 12 patients complained of loss of hearing; of these, only 7 were found to have defective hearing. No relationship was found between the decrease in hearing and the severity of the disease.

FRANKEL, Philadelphia.

INTRACRANIAL OSTEOCHONDROMA. R. W. FORSYTHE, G. S. BAKER, M. B. DOCKERTY and J. D. CAMP, Proc. Staff Meet., Mayo Clin. **22**:350 (Aug. 20) 1947.

The authors report the case of an intracranial osteochondroma with a meningeal attachment. The patient, a white man aged 51, was first seen in September 1939, when he complained of nocturia, dysuria, frequency of micturition, pain in the perineal region extending into both legs, pain in the lower part of the back and occasional headache. Examination disclosed a right inguinal hernia, injection of the nasopharynx and slight benign hypertrophy of the prostate gland with minimal symptoms of obstruction. The patient was discharged, returning in August 1946, years later. At this time he complained of fatigue; generalized aching, especially in the shoulders; difficulty in moving the shoulders after waking during the night; insomnia, and occasional stiffness of the fingers, present since early in 1945. The interim history revealed two infections of the urinary tract, which had been treated with sulfonamide compounds. Roentgenologic studies at this time revealed only a large, calcified mass in the right posteroparietal area. After his transfer to the department of neurology, there was elicited the history of periodic right-sided headaches, with occasional vertigo, of ten years' duration. In April 1945 the patient had received an injury to the head, from which he was unconscious for ten to fifteen minutes and sustained a laceration of the scalp; there were no sequelae. Bilateral tinnitus had become apparent in August 1940. Neurologic examination revealed postural vertigo and a tremor of both hands during rest and on movement, both of which symptoms were mild; there was no other neurologic sign. Operation revealed an osteochondroma, which had probably originated in the dura and falx cerebri; the tumor was removed piecemeal. Cranioplasty with tantalum was accomplished. Neurologic examination then showed a normal status. The patient was again seen four months later because of an inflammatory lesion of the left testis; at that time there were no complaints or symptoms referable to the cranium.

FRANKEL, Philadelphia.

EVALUATION OF THE PRESENCE OF POLYMORPHONUCLEAR NEUTROPHILS IN THE SPINAL FLUID WITHOUT PLEOCYTOSIS. J. B. DOS REIS, Arq. de neuropsiquiat. **5**:225 (Sept.) 1947.

Dos Reis found increased neutrophils in the spinal fluid with a normal cell count in 40 of 1,414 specimens of the spinal fluid. A cell count of above 3 per cubic millimeters was considered abnormal. There were 11 cases of vascular accident without a bloody spinal fluid. The cell count varied from 0.4 to 4 cells per cubic millimeter, with the incidence of neutrophils ranging from 4 to 91 per cent. In 1 of the cases, later puncture revealed no neutrophils. In 6 cases of status epilepticus the cell count of the spinal fluid varied from 0.2 to 12, with 2 to 51 per cent neutrophils. In 1 case the percentage of neutrophils dropped from 51 to 5 per cent one day after the first puncture; in this case there were 12 cells per cubic millimeter of spinal fluid. In 4 cases of head injury without bloody spinal fluid, the cell count varied from 0.8 to 1.8 per cubic millimeter, with the percentage of neutrophils ranging from 9 to 60. In 4 cases of cerebral tumor, with a cell count of from 0.4 to 4.4 per cubic millimeter, the neutrophils varied from 2 to 10 per cent. In 6 cases of toxic-infectious psychoses and in 2 cases in which changes in the nervous system accompanied anemia, a similar increase in the percentage of neutrophils was observed. In 1 of 7 cases of induced insulin coma, the neutrophil count was 1 per cent. In 2 cases of prolonged insulin coma, 44 and 29 per cent neutrophils, respectively, were present, without any increase in cells in the spinal fluid. Such increase in neutrophils is due to local circulatory disturbances in the brain, and in some cases is the only evidence on examination of the spinal fluid of the existence of a pathologic process.

N. SAVITSKY, New York.

Treatment, Neurosurgery

SYPHILITIC ARACHNOIDITIS TREATED WITH PENICILLIN. J. LAMAR CALLAWAY, RAY O. NOOJIN, BEATRICE H. KUHN, KATHLEEN A. RILEY and JOHN A. SEGERSON, Am. J. Syph., Gonor. & Ven. Dis. **30**:231 (May) 1946.

The authors report 2 cases of syphilitic arachnoiditis. One patient was followed for eight months and the other for nine month. Each patient received 4,000,000 units of penicillin intramuscularly.

Although no specific conclusions can be based on the improvement noted in these 2 cases, the authors feel "that the results justify further investigation of the use of large doses of penicillin in the treatment of syphilitic arachnoiditis."

GUTTMAN, Philadelphia.

INTRATHECAL ADMINISTRATION OF PENICILLIN IN GENERAL PARESIS. GEORGE D. WEICKHARDT, Am. J. Syph., Gonor. & Ven. Dis. **30**:235 (May) 1946.

This is a preliminary report on 5 patients who had dementia paralytica and were treated with penicillin administered solely by the intrathecal route.

Of the 5 patients treated, none had serious reactions attributable to the intrathecal injections of penicillin, although 2 received a total of 850,000 units within the ten day period. Three patients were given doses as large as 100,000 units on several consecutive days, without untoward affect. A febrile response (probably a Herxheimer reaction) followed the initial dose in 4 of the 5 patients. One patient died after the eighth injection, of 125,000 units. Autopsy showed that death was due to suffocation by food. The gross and microscopic examination of the brain and spinal cord of this patient failed to reveal changes which could be ascribed to this form of intrathecal medication.

The authors state that the clinical and serologic results so far observed in the 4 surviving patients compare favorably with those seen after accepted methods of treatment. The 4 patients who survived showed serologic, as well as clinical, improvement. The follow-up study has been conducted for a year. The authors state that this method, which consists in a gradual daily elevation of the dose of penicillin, up to 100,000 units per day, seems to be safe but is still in the experimental stage.

GUTTMAN, Philadelphia.

RADICAL SURGERY AND PENICILLIN IN BRAIN ABSCESS. JACQUES LEBEAU, J. Neurosurg. **3**:359 (Sept.) 1946.

LeBeau reports on the results of treatment of 17 patients with brain abscess by complete primary extirpation. Three patients who were not given penicillin did not survive. The remaining 14, including 3 with thoracogenic abscess, were all cured in a one stage procedure, followed by postoperative administration of an antibiotic. The abscesses, both acute and chronic, were treated by complete removal of the abscess, with all the inflammatory brain tissue surrounding it. After operation, 20,000 units of penicillin was put in the abscess bed; the same amount was injected into the ventricles; 20,000 units was placed under the flap for four days, and 200,000 units was injected daily intravenously or intramuscularly for four days. If gram-negative bacilli were present, sulfadiazine was given. Postoperative meningitis was not encountered, even though the operation required opening the abscess, and often the ventricle.

TOZER, Philadelphia.

SEPARATION AT THE SUTURE SITE AS A CAUSE OF FAILURE IN REGENERATION OF PERIPHERAL NERVES. BENJAMIN B. WHITCOMB, J. Neurosurg. **3**:399 (Sept.) 1946.

Whitcomb analyzed the results of 605 nerve sutures performed by various surgeons at Army neurosurgical centers. The commonest cause of failure of complete regeneration was separation at the site of the anastomosis. Predisposing factors in this separation were: (1) individual elasticity of nerves, (2) fibrosis and fixation of nerves, (3) length of separation, (4) time interval between injury and repair and (5) suture material used. Fine tantalum wire was advocated for either direct or stay sutures. If a nonmetallic material is used for suturing, metallic markers should be placed on each segment of the nerves. Since they are opaque to roentgen rays, the markers give a prompt and accurate estimation of the integrity of the suture site without one's waiting for the clinical signs of nonunion. The sciatic and peroneal nerves had a higher incidence of disruption after suturing. In all cases the ruptured suture site should be reexplored and every effort exerted to correct the defect.

TOZER, Philadelphia.

ANTERIOR RHIZOTOMY: THE ACCURATE IDENTIFICATION OF MOTOR ROOTS AT THE LOWER END OF THE SPINAL CORD. I. B. MACDONALD, K. G. MCKENZIE and E. H. BOTTERELL, J. Neurosurg. **3**:421 (Sept.) 1946.

Macdonald, McKenzie and Botterell point out that in performing anterior rhizotomy it is difficult to identify specific motor roots of the lumbosacral portion of the spinal cord. The method based on visualization of the dentate ligament and determination of the first lumbar posterior root is inaccurate because the lower attachment of the ligament varies widely, as shown by the authors' anatomic study.

The authors also show that the lowest large root to leave the conus medullaris is the first sacral motor root. Anterior rhizotomy in patients with spastic paralysis occasionally causes disturbances in reflex bladder control. This may be due to section of the first sacral root or, more likely, to interference with the blood supply of the conus medullaris. Therefore, attempts should be made to spare arteries accompanying anterior motor roots.

TOZER, Philadelphia.

ANALYSIS OF SURGICAL FAILURES AND FATALITIES FOLLOWING THORACOLUMBAR SYMPATHECTOMY FOR ESSENTIAL HYPERTENSION. J. W. HINTON and J. W. LORD JR., New York State J. Med. **46**:1714 (Aug. 1) 1946.

During the past four years, Hinton and Lord have operated on 227 patients for hypertensive vascular disease, 152 being operated on by the Smithwick technic. Beginning in June 1945, the authors extended the operation to the higher thoracic ganglia, and by December 1945 they were removing ganglia from the third thoracic to the second lumbar, inclusive, in most operations, and always through the fourth thoracic ganglion. Twenty-six of the 227 patients died, a mortality of 11.5 per cent. The immediate mortality was higher in the more extensive operative procedure. The fatalities were divided into three groups. In group 1, 5 of 15 cases, all four major organs—eyes, cerebral vessels, heart and kidneys—were involved. If the degree of involvement in each organ is graded from 1 to 4 plus, it is found that these 15 cases had an average grade of 12.5 plus, out of a maximum of 16. Operative procedure in these cases indicated poor judgment. In group 2, of 7 cases, three organs were involved, with an average score of 8 plus. In group 3, of 4 cases, two organs were involved, with an average grade of 8 plus. In the last two groups there was some justification for operation, as the organs were not completely damaged by the long-standing hypertensive vascular disease. The authors think that when the degree of involvement in all organs exceeds 8 plus it is questionable whether a thoracolumbar sympathectomy will give lasting results.

J. A. M. A.

CURARE IN THE TREATMENT OF POLIOMYELITIS. ROBERT L. RICHARDS, EARL C. ELKINS and KENDALL B. CORBIN, Proc. Staff Meet., Mayo Clin. **22**:31 (Jan. 22) 1947.

Curare was administered intramuscularly alone or in oil, or intravenously with or without "pentothal sodium" to 18 patients in the acute stages of poliomyelitis. In some cases more than one method of administration was employed. All patients also received the accepted treatment with hot packs and physical therapy. "The results indicate that treatment with curare does not materially affect any aspect of the clinical course of the disease. From the standpoint of shortening convalescence, curare did little or nothing more than that expected from the physical procedures."

ALPERS, Philadelphia.

ENCEPHALOCRANIAL TRAUMATISM: NEW TREATMENT OF CEREBRAL EDEMA: PRELIMINARY REPORT. E. FUENTES BESOAÍN, Rev. méd. de Chile **74**:340 (May) 1946.

In the treatment of post-traumatic cerebral edema, Fuentes Besoaín used Schemm's method, which consists in institution of an acidotic diet without chlorides and the administration of large quantities of fluid. He has used this treatment in more than 20 cases, 2 of which are reported. Consciousness returns more rapidly with this than with other treatments. Diuresis begins to increase from twelve to twenty-four hours after the treatment is begun, and a decrease in head-

ache and nausea accompanies the augmentation in diuresis. The psychologic condition of these patients is much better than when the water intake is limited. The treatment is usually continued for three or four days after the subjective symptoms have disappeared. Total recovery usually requires between six and twelve days.

J. A. M. A.

Encephalography, Ventriculography, Roentgenography

Observations on Encephalographic Findings in Cerebral Trauma. Charles E. Troland, Donald H. Baxter and Richard Schatzki, J. Neurosurg. **3**:390 (Sept.) 1946.

Troland, Baxter and Schatzki report on 261 patients given lumbar encephalographic examinations at an Army neurologic and neurosurgical center. Of these, 206 had cranial trauma, 177 having defects of the skull and 29 closed head injuries. Three fourths of the patients had abnormal encephalograms, characterized by (1) unilateral dilatation of the ventricles, 29 per cent; (2) bilateral, asymmetric enlargement of the ventricles, 29 per cent; (3) bilateral, symmetric enlargement of the ventricles, 16 per cent.

Follow-up encephalograms on the second day in 60 cases showed increased ventricular size in over 30 per cent. The authors conclude that ventricular enlargement can be demonstrated, in a majority of cases, as soon as cerebral edema, consequent to head injury, had subsided. The enlargement is mainly due to loss of brain substance, probably lipids, with a resulting shift of the remaining brain tissue and ventricles toward the atrophied side.

Tozer, Philadelphia.

Congenital Familial Anhidrosis and Neurolabyrinthitis. H. F. Helweg-Larsen and K. Lüdvigsen, Acta dermat.-venereol. **26**:489 (May) 1946.

Helweg-Larsen and Ludvigsen describe a Swedish family 14 members of which had congenital anhidrosis (intensified hypohidrosis). Diminished sweat secretion was noticed in the affected members of the family from the age of 1 year. Instead of sweat drops, granular or ring-formed salt formation appeared on the skin, being most conspicuous on the ridge of the nose, on the upper part of the neck and in the axillas. Subjectively, the patients felt uncomfortable in the heat, and in summer they had to quit work on account of a sensation of heat, oppressive headache, dyspnea and palpitation. Biopsy of skin from the right forearm showed absence of sweat glands or the excretory ducts of sweat glands. On exposure to a temperature of 127.4 F. (53 C.) for fifty minutes, large and scattered sweat points appeared, most of them localized in the axilla and in the pectoral region; these spots gradually presented a ringlike appearance. Biopsy of the skin revealed a single, definitely hypertrophic sweat gland with high columnar epithelium, corresponding to one of the annular sweat marks in the axillary fold. The patients did not present dental anomalies, defective development of hair, ozena or cranial deformities. Neurolabyrinthitis occurred in these patients between the ages of 35 and 45 years. Because of the ectodermal origin of the labyrinth, the possibility of a common predisposition to the labyrinthitis and the anhidrosis is to be considered. In contrast to hypotrichotic anhidrosis, the anhidrosis in the authors' cases was transmitted by simple dominant inheritance. The authors suggest an autosomal morbid factor, different from that for hypotrophic anhidrosis, which may have a pleiotropic effect on the development of the sweat glands and the labyrinths.

J. A. M. A.

Book Reviews

Take up Thy Bed and Walk. By David Hinshaw. Price, $2.75. Pp. 262, with illustrations. New York: G. P. Putnam's Sons, 1948.

This book is a popular presentation of achievements in the new and exciting field of rehabilitation, written primarily for the layman. The author emphasizes particularly the historical development of the field and the modern concept of rehabilitation of the physically handicapped.

The changing concepts during the past thirty years, particularly the development of teamwork of a group of professional workers and the emphasis on treating the whole person, are brought into focus by detailed description of the history of the Institute for the Crippled and Disabled in New York city from 1917 to the present time. This organization has taken a leading role in the development of ideas and programs in the field of rehabilitation and has pioneered in creating possibilities for improvement of the severely handicapped, who were formerly considered not feasible for rehabilitation.

The outstanding accomplishment of the armed services and the Veterans Administration in rehabilitation of the war injured during and after the recent war is well known, but the role of the Institute in training personnel for these programs and in initiating and helping to set up the basic pattern for rehabilitation in World War II is of considerable interest.

The modern rehabilitation center requires the cooperative efforts of doctors, physical therapists, occupational therapists, medical and psychiatric social workers, psychologists, vocational counselors, teachers and employment specialists. It must be a highly organized institution and must have the cooperation of public and private agencies in the community, as well as employers and labor organizations. Every large community needs such a rehabilitation center, and the fragmentary efforts of interested physicians and other professional workers, working individually, to do their bit toward rehabilitation of the physically handicapped has been a failure.

It is no longer enough to provide medical and surgical care to reduce or minimize the physical disability. Equally important may be the psychosocial adjustment of the patient and the vocational counseling and training, which can be successful only if it achieves economic independence and security in a job. The handicapped person must be able to compete on equal terms with his able-bodied fellow worker. There must be no hint of charity in the employment of the handicapped. The results of repeated surveys have shown that, when placed in the proper job for which he has acquired the necessary skill, the handicapped worker compares very favorably with the normal one. These facts are not sufficiently widely known among employers, so that the handicapped are still the last to be hired and the first to be fired and are more subject to fluctuations in total employment than are other workers.

The handicapped veteran has opportunities today which were beyond the fondest dreams of similar patients injured in World War I. He is given all necessary medical and surgical care, helped in psychosocial adjustment, given vocational counseling and training and offered every assistance in finding a suitable job. While similar programs are also available to the handicapped civilian, particularly through the Office of Vocational Rehabilitation of the Federal Security Agency,

the funds available to the Agency are so limited that only a small proportion of persons who would benefit from the program are being assisted. This is a tragic waste, for not only is it a loss to the community, and to the nation in dollars, and cents to have a disabled person unemployed who could be made employable through treatment and training, but it is also a tremendous loss in terms of the self respect and dignity of the disabled person. Despite the good work that the Office of Vocational Rehabilitation is doing, this organization is reaching so few of those who need its services that it is far from rehabilitating each year the number of persons who become handicapped annually in this country.

One of the most interesting features of the historical development of rehabilitation in the United States has been the backwardness of members of the medical profession in providing leadership in this important field. The early efforts at rehabilitation of the handicapped were aimed primarily at vocational training. The federal-state vocational rehabilitation program is still administered entirely through state departments of education, rather than of health. For many years the vocational rehabilitation program provided solely for vocational training, and it was not until 1943 that a revision of the federal law included physical restoration services as an integral part of the program, as well as psychiatric treatment of the mentally handicapped. Although the Institute for the Crippled and Disabled was established in 1917, not until 1940 was it found necessary to employ a medical director. At one time the Institute was invited to join with an outstanding medical center and hospital and the trustees favorably considered this move, but the patients at the Institute, because of their unfavorable experiences at hospitals, voted unanimously against affiliation with the hospital. Mr. Hinshaw favors nonmedical leadership in rehabilitation of the handicapped. In my opinion, only medical direction of the program will carry to fruition the full potentialities of the field of rehabilitation. This medical leadership must be provided by physicians specially trained in this field. There must be not only the highly organized teamwork between the members of different professions but, equally important, effective teamwork among the various specialties of medicine and surgery. While great strides have been made by following the philosophy of looking at the man's abilities rather than his disabilities, even more gratifying results can be achieved by intensive medical treatment first to eliminate or minimize the handicap and only later to develop the patient's abilities to their full potentialities.

The Case of Rudolf Hess. Edited by J. R. Rees, M.D. Price, $3. Pp. 224. New York: W. W. Norton & Company, Inc., 1948.

The case of Rudolf Hess was a "top secret" incident of World War II and was studied by a group of eminent psychiatrists. This book is an excellent bit of insight into the Hitlerian government, which could admit a bizarre mentality like Rudolf Hess's into its highest circle.

From the landing in Scotland through the Nuremberg trial, the case of Hess is carefully handled; American, British, French and Russian psychiatrists are cited. There were attempts at psychotherapy and narcosynthesis; however, they failed. The reader can sense the frustration experienced in trying to unlock the military secrets in this mind.

At Nuremberg, the question was raised, "Is Hess psychotic?" The psychiatrists did not think so. Yet he shows many symptoms of schizophrenia. In the words of the author, "In this book we have tried, in Adolf Meyer's words, not to sort out the patient but the facts. This we have endeavored to do faithfully, and

we may safely leave the problem of final diagnosis to the predilection and judgment of our colleagues, present and future."

This book is an excellent case study and will be profitable reading.

Total Protein, Globulin and Albumin in Lumbar Fluid in Cryptogenic Epilepsy. By Richard Eeg-Olofsson. Acta psychiatrica et neurologica, Supplement 50. Pp. 192. Stockholm: Sweden, Ivar Hæggström, 1948.

The author has measured the total protein and globulin-albumin quotient in 133 cases of epilepsy (21 of the "symptomatic" type) and in 67 control cases. The data are presented in detail in 15 tables and 4 charts and are discussed intelligently against a background of more than 200 references. The method of Izikowitz was employed. In 5.5 per cent of 100 cases of cryptogenic epilepsy, the total protein was above the normal limit of 65 mg. per hundred cubic centimeters for males and 49 mg. for females. Among the male subjects, mean values were as follows: cryptogenic epilepsy, 41.32 mg.; symptomatic epilepsy, 38.71 mg.; normal subjects (Izikowitz), 39.46 mg., per hundred cubic centimeters. In the same groups, the globulin-albumin quotient was below normal (0.14 for male and 0.13 for female patients) in 10 per cent. The mean quotient for male patients with cryptogenic epilepsy was 0.2103, for male patients with symptomatic epilepsy, 0.2181, and for normal male subjects, 0.2427. This abnormal ratio was due both to unusually low values for globulin and to high values for albumin.

Measurements on successive occasions might produce different values. Thus, a subnormal quotient was found at least once in 17 per cent of 110 patients. However, abnormalities could not be related to the time interval after a seizure, to the frequency of attacks, to the duration of the epilepsy or to electroencephalographic foci. Although some of the case histories give evidence of the presence of lesions of the brain, the author seems to suggest an etiologic role for the protein by proposing the term "epilepsia hyperproteinorrhachia."

The low globulin-albumin ratios are not due to low values for total protein, nor are they confined to cases of cryptogenic epilepsy. They may be related to alterations in the permeability of the blood–spinal fluid barrier. The author is not satisfied with present methods of analysis and hopes for additional evidence from electrophoresis. He believes that the results justify further study. This is a painstaking, though somewhat disconnected, presentation of a mass of clinical and laboratory data. The author has difficulty in deciding whether certain cases should be classified under symptomatic or cryptogenic epilepsy. Apparently, he does not consider that in a given case both types may be present.